10/048022 JC07 Rec'd PCT/PTO 28 JAN 2002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
REQUEST FOR FILING NATIONAL PHASE OF PCT APPLICATION UNDER 35 U.S.C. 371 AND 37 CFR 1.494 OR 1.495

To: Hon. Commissioner of Patents
Washington, D.C. 20231

00909

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)

Atty Dkt: P 0290430 /Z70564/UST
M# /Client Ref.

From: Pillsbury Winthrop LLP, IP Group:

Date: January 28, 2002

This is a **REQUEST** for FILING a PCT/USA National Phase Application based on:

1. International Application	2. International Filing Date	3. Earliest Priority Date Claimed
PCT/US00/20401	27 July 2000	27 July 1999
⇧ country code	Day MONTH Year	Day MONTH Year (use item 2 if no earlier priority)

4. Measured from the earliest priority date in item 3, this PCT/USA National Phase Application Request is being filed within:

   (a) ☐ 20 months from above item 3 date (b) ☒ 30 months from above item 3 date,

   (c) Therefore, the due date (unextendable) is January 27, 2002

5. Title of Invention Analysis and Pattern Recognition in Large, Multidimensional Data Sets Using Low-Resolution Data Grouping

6. Inventor(s) Charles Lerman

Applicant herewith submits the following under 35 U.S.C. 371 to effect filing:

7. ☒ Please immediately start national examination procedures (35 U.S.C. 371 (f)).

8. ☒ **A copy of the International Application** as filed (35 U.S.C. 371(c)(2)) is transmitted herewith (file if in English but, if in foreign language, file only if not transmitted to PTO by the International Bureau) including:

   a. ☒ Request;
   b. ☒ Abstract;
   c. 82 pgs. Spec. and Claims;
   d. 64 sheet(s) Drawing which are ☐ informal ☒ formal of size ☒ A4 ☐ 11"

9. ☒ **A copy of the International Application has been transmitted by the International Bureau.**

10. **A translation of the International Application** into English (35 U.S.C. 371(c)(2))
    a. ☐ is transmitted herewith including: (1) ☐ Request; (2) ☐ Abstract;
       (3) ______ pgs. Spec. and Claims;
       (4) ______ sheet(s) Drawing which are:
       ☐ informal ☐ formal of size ☐ A4 ☐ 11"
    b. ☒ is not required, as the application was filed in English.
    c. ☐ is not herewith, but will be filed when required by the forthcoming PTO Missing Requirements Notice per Rule 494(c) if box 4(a) is X'd or Rule 495(c) if box 4(b) is X'd.
    d. ☐ Translation verification attached (not required now).

RE: USA National Phase Filing of PCT /US00/20401

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11. ☒ Please see the attached Preliminary Amendment

12. ☐ Amendments to the claims of the International Application **under PCT Article 19 (35 U.S.C. 371(c)(3)), i.e., before 18th month from first priority date above in item 3, are transmitted herewith (file only if in English) including:**

13. ☒ PCT Article 19 claim amendments (if any) have been transmitted by the International Bureau

14. ☐ Translation of the amendments to the claims **under PCT Article 19 (35 U.S.C. 371(c)(3)), i.e., of claim amendments** made before 18th month, **is attached (required by 20th month from the date in item 3 if box 4(a) above is X'd, or 30th month if box 4(b) is X'd, or else amendments will be considered canceled).**

15. **A declaration of the inventor** (35 U.S.C. 371(c)(4))
   a. ☐ is submitted herewith ☐ Original ☐ Facsimile/Copy
   b. ☒ is not herewith, but will be filed when required by the forthcoming PTO Missing Requirements Notice per Rule 494(c) if box 4(a) is X'd or Rule 495(c) if box 4(b) is X'd.

16. **An International Search Report (ISR):**
   a. Was prepared by ☒ European Patent Office ☐ Japanese Patent Office ☐ Other
   b. ☒ has been transmitted by the international Bureau to PTO.
   c. ☒ copy herewith (3 pg(s).) ☐ plus Annex of family members (_ pg(s).).

17. **International Preliminary Examination Report** (IPER):
   a. ☒ has been transmitted (if this letter is filed after 28 months from date in item 3) in English by the International Bureau with Annexes (if any) in original language.
   b. ☐ copy herewith in English.
   c.1 ☐ IPER Annex(es) in original language ("Annexes" are amendments made to claims/spec/drawings during Examination) including attached amended:
   c.2 ☐ Specification/claim pages #__ claims #
   Dwg Sheets #
   d. ☐ Translation of Annex(es) to IPER **(required by 30th month due date, or else annexed amendments will be considered canceled).**

18. **Information Disclosure Statement** including:
   a. ☐ Attached Form PTO-1449 listing documents
   b. ☐ Attached copies of documents listed on Form PTO-1449
   c. ☒ A concise explanation of relevance of ISR references is given in the ISR.

19. ☐ **Assignment** document and Cover Sheet for recording are attached. Please mail the recorded assignment document back to the person whose signature, name and address appear at the end of this letter.

20. ☐ Copy of Power to IA agent.

21. ☐ **Drawings** (complete only if 8d or 10a(4) not completed): _ sheet(s) per set: ☐ 1 set informal; ☐ Formal of size ☐ A4 ☐ 11"

22. Small Entity Status ☒ is **Not** claimed ☐ is claimed (**pre**-filing confirmation required)

22(a) __ (No.) Small Entity Statement(s) enclosed (since 9/8/00 Small Entity Statements(s) not essential to make claim)

23. **Priority** is hereby claimed under 35 U.S.C. 119/365 based on the priority claim and the certified copy, both filed in the International Application during the international stage based on the filing in (country) United States of America of:

	Application No.	Filing Date		Application No.	Filing Date
(1)	09/361,122	27 July 1999	(2)		
(3)			(4)		
(5)			(6)		

   a. ☒ See Form PCT/IB/304 sent to US/DO with copy of priority documents. If copy has not been received, please proceed promptly to obtain same from the IB.
   b. ☐ Copy of Form PCT/IB/304 attached.

RE: USA National Phase Filing of PCT/US00/20401

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24. Attached:

25 Per Item 17.c2, **cancel original** pages #___, claims #___, Drawing Sheets #

26. **Calculation of the U.S. National Fee (35 U.S.C. 371 (c)(1)) and other fees is as follows:**
Based on amended claim(s) per above item(s) ☐ 12, ☐ 14, ☐ 17, ☐ 25 (hilite)

Total Effective Claims	48	minus 20 =	28	x $18/$9	=	$504	966/967
Independent Claims	9	minus 3 =	6	x $84/$42	=	$504	964/965
If any proper (ignore improper) Multiple Dependent claim is present,				add$280/$140		+	968/969

BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(4)): →→ **BASIC FEE REQUIRED, NOW** →→→→

A. If country code letters in item 1 are **not** "US","BR","BB","TT","MX","IL" "NZ", "IN" or "ZA"

See item 16 re:

1. Search Report was not prepared by EPO or JPO --------- add$1,040/$520 — 960/961
2. Search Report was prepared by EPO or JPO ------------ add$890/$445 — +0 — 970/971

SKIP B, C, D AND E UNLESS country code letters in item 1 are "US","BR","BB","TT","MX","IL", "NZ", "IN", "ZA", "LC" or "PH"

(X) → ☒ B. If USPTO did not issue both International Search Report (ISR) and (if box 4(b) above is X'd) the International Examination Report (IPER), ------------------- add$1,040/$520 — +1040 — 960/961

(only) (one) (of) → ☐ C. If USPTO issued ISR but not IPER (or box 4(a) above is X'd), ------------------------------------ add$740/$370 — +0 — 958/959

(these) (4) (boxes) → ☐ D. If USPTO issued IPER but IPER Sec. V boxes not all 3 YES, ---------------------------------- add$710/$355 — +0 — 956/957

→ ☐ E. If international preliminary examination fee was paid to USPTO and Rules 492(a)(4) and 496(b) satisfied (in IPER Sec. V all 3 boxes must be YES for all claims), -- add $100/$50 — +0 — 962/963

27. **SUBTOTAL =** $2,048

28. If Assignment box 19 above is X'd, add Assignment Recording fee of ----$40 — +0 — (581)

29. If box 15a is x'd, determine whether inventorship on Declaration is different than in international stage. If yes, add (per Rule 497(d) ----$130 — +0 — (098)

30. Attached is a check to cover the ------------------------ **TOTAL FEES** $2,048

Our Deposit Account No. 03-3975
Our Order No. 009901 (C#) | 0290430 (M#)

00909

CHARGE STATEMENT: The Commissioner is hereby authorized to charge any fee specifically authorized hereafter, or any missing or insufficient fee(s) filed, or asserted to be filed, or which should have been filed herewith or concerning any paper filed hereafter, and which may be required under Rules 16-18 and 492 (missing or insufficient fee only) now or hereafter relative to this application and the resulting Official document under Rule 20, or credit any overpayment, to our Account/Order Nos. shown above for which purpose a duplicate copy of this sheet is attached.
This CHARGE STATEMENT does not authorize charge of the issue fee until/unless an issue fee transmittal form is filed

Pillsbury Winthrop LLP
Intellectual Property Group

By Atty: **Paul L. Sharer** **Reg. No.** **36004**
Sig: [signature] **Fax:** **(703) 905-2500**
Atty/Sec: PLS/kmh **Tel:** **(703) 905-2180**

NOTE: File in duplicate with 2 postcard receipts (PAT-103) & attachments.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT APPLICATION OF

Inventor(s): Charles Lerman

Filed: January 28, 2002

Title: *ANALYSIS AND PATTERN RECOGNITION IN LARGE, MULTIDIMENSIONAL DATA SETS USING LOW-RESOLUTION DATA GROUPING*

PRELIMINARY AMENDMENT

Hon. Commissioner of Patents
Washington, D.C. 20231

Sir:

Prior to prosecution on the merits, please amend this application as follows herein.

IN THE SPECIFICATION

Please insert the following heading and paragraph after the title of the application on page 1 of the specification:

--Cross Reference to Related Applications

This application is a national phase application based on PCT/US00/20401, filed July 27, 2000, and which further claims priority from U.S. Application No. 09/361,122, filed July 27, 1999. These applications are incorporated herein by reference.--

IN THE CLAIMS

Kindly amend the claims as follows:

7. (Amended) A method as in claim 3, wherein the breakpoints are selected from (a) numeric values; and (b) textual values.

13. (Amended) A method according to claim 11, wherein the data comprises a number of parameters for each of a number of cases and the scoring rule comprises a scoring function of user-selectable parameters and user-defined weights for the selected parameters to be used in scoring the cases, wherein the scoring of the grouped data comprises:

    applying the function to the data to obtain a score for each case.

23. (Amended) A system as in claim 19, wherein the breakpoints are selected from: (a) numeric values; and (b) textual values.

29. (Amended) A system according to claim 27, wherein the data comprises a number of parameters for each of a number of cases and the scoring rule comprises a scoring function of user-selectable parameters and user-defined weights for the selected parameters to be used in scoring the cases, wherein the mechanism constructed and adapted to score of the grouped data comprises:

a mechanism constructed and adapted to apply the function to the data to obtain a score for each new case.

39. (Amended) A medium as in claim 35, wherein the breakpoints are selected from: (a) numeric values; and (b) textual values.

45. (Amended) A medium according to claim 43, wherein the data comprises a number of parameters for each of a number of cases and the scoring rule comprises a scoring function of user-selectable parameters and user-defined weights for the selected parameters to be used in scoring the cases, wherein the scoring of the grouped data comprises:

applying the function to the data to obtain a score for each case.

Please refer to the attached Appendix for changes made to the above claims.

REMARKS

The present amendment adds reference to the priority applications to the specification and further amends Claims 7, 13, 23, 29, 39 and 45 to remove multiple dependencies from the claims. No new matter has been added.

Favorable action on the merits is respectfully requested.

Respectfully submitted,

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Date: January 28, 2002
Attorney Reference: 009901/0290430

Attachment: Appendix

APPENDIX: VERSION TO SHOWS CHANGES MADE TO APPLICATION

In the Claims

The claims were amended as follows:

7. (Amended) A method as in [any one of claims 3 and 6] claim 3, wherein the breakpoints are selected from (a) numeric values; and (b) textual values.

13. (Amended) A method according to claim 11 [or 12], wherein the data comprises a number of parameters for each of a number of cases and the scoring rule comprises a scoring function of user-selectable parameters and user-defined weights for the selected parameters to be used in scoring the cases, wherein the scoring of the grouped data comprises:

applying the function to the data to obtain a score for each case.

23. (Amended) A system as in [any one of claims 19 and 22] claim 19, wherein the breakpoints are selected from: (a) numeric values; and (b) textual values.

29. (Amended) A system according to claim 27 [or 28], wherein the data comprises a number of parameters for each of a number of cases and the scoring rule comprises a scoring function of user-selectable parameters and user-defined weights for the selected parameters to be used in scoring the cases, wherein the mechanism constructed and adapted to score of the grouped data comprises:

a mechanism constructed and adapted to apply the function to the data to obtain a score for each new case.

39. (Amended) A medium as in [any one of claims 35 and 38] claim 35, wherein the breakpoints are selected from: (a) numeric values; and (b) textual values.

45. (Amended) A medium according to claim 43 [or 44], wherein the data comprises a number of parameters for each of a number of cases and the scoring rule comprises a scoring function of user-selectable parameters and user-defined weights for the selected parameters to be used in scoring the cases, wherein the scoring of the grouped data comprises:

applying the function to the data to obtain a score for each case.

Analysis and Pattern Recognition in Large, Multidimensional Data Sets Using Low-Resolution Data Grouping

1. Field of the Invention

This invention relates to analysis and pattern recognition of data. More particularly, this invention relates to methods, systems and devices and combinations thereof for analysis and pattern recognition in large sets of multidimensional data using low-resolution data grouping.

2. Background

With the advent of computerization and the low cost of data storage and acquisition, people in many endeavors are now accumulating very large sets of data. For example, scientists in drug and chemical companies now use automation to perform so-called high-throughput screening ("HTS") of chemical compounds. HTS uses automated, relatively low-cost techniques to obtain various items of information about chemical compounds. The goal of using HTS is to obtain information about a very large number of compounds in a quick and relatively low-cost manner. Having accumulated a very large HTS data set, it is necessary to evaluate the data in order to determine which, if any, of the analyzed

compounds warrants further investigation. However, the results of such HTS tend to be very large sets of multidimensional data, on the order of thousands of rows and dozens of columns, and so it is very difficult to make decisions just by looking at the data.

In addition to the very large amounts of data produced by HTS, difficulties in existing data handling and analysis methods include the following:

- Data comes from very diverse sources, including HTS laboratories, physical measurements, bio-scientists' laboratories, various computational software programs, etc., and the different sources tend to have very diverse kinds of output including numbers, text, mixed data types, error notations, blank data, replicate data (more than one value per compound), etc.
- Not all sources produce data on the same list of compounds, or in the same order.
- Some data values are misleadingly too precise, i.e., have high relative experimental errors or noise, and can easily be over-interpreted.
- Medicinal chemists have to weigh very different kinds of factors (for example, molecular weight vs. dose-responsiveness vs. ClogP vs. secondary biology vs. selectivity across screens) in trying to determine which are the best compounds or clusters of compounds to which to devote further work.

SUMMARY OF THE INVENTION

This invention solves the above and other problems by providing automated tools to help with and speed up these data handling and analysis processes. These tools embody some assumptions about how the data should be treated by internalizing the most generally acceptable assumptions, but leaving more idiosyncratic decisions to individual users.

A central concept on which this invention is based is grouping data into a relatively small number of categories using low-resolution data grouping. The grouping is visualized by assigning colors to data groups, e.g., in spreadsheets. Grouping of data potentially changes the precision of the data.

This categorization of data has several major benefits, including:

- creating a visual means of finding data patterns;
- beneficially blurring small variations in numerical data that are, in practice, excessively fine distinctions, possibly due to experimental error; and
- providing, in the colors themselves, a means or "common currency" to evaluate candidates across a wide range of data types.

Accordingly, in one aspect, this invention provides mechanisms to expedite pattern recognition in large sets of multidimensional data, such as those that chemists assemble when evaluating hits from high-throughput screening (HTS) and deciding which ones will get priority for further investigation. In controlled trials, this invention has reduced the time to evaluate real data sets, from days of intense human effort, which is vulnerable to errors due to volume or fatigue, to a few minutes of automation with graphical presentation of results.

It quickly becomes obvious upon using the system that the tools also have value in data-handling areas other than HTS. Examples include selection and management of any kind of tabulated data, e.g., portfolio management for any kind of rated portfolios, selection of drug candidate compounds, selection and management of proteins that are candidates for targets for drugs, selection and management of research projects competing for resources, and evaluating employee performance or job candidates.

The system of this invention includes a new special command menu, a set of graphical user interface worksheets, and action buttons to facilitate the coloring and color analysis processes for the user. While the central process is the data grouping and coloring, there are also new tools for the upstream, or pre-grouping and coloring processes of importing, assembling, regularizing, and characterizing data in a spreadsheet, and for the downstream processes of visualizing, scoring, comparing, and sorting large amounts of color-coded data. The data-grouping and spreadsheet-coloring tool is presently implemented with a flexible, powerful, and convenient user interface that does not require knowledge of spreadsheet macros or of the Visual Basic language (used for the system's implementation).

Accordingly, this invention provides methods, systems and devices for operating on data.

In one aspect, the method of this invention provides at least one user-defined grouping rule for grouping the data into a user-definable number of groups. At least one of the grouping rules is applied to the data. The data may be provided in a table and the grouping rule applies to at least one user-selectable column of the table. In some embodiments, the grouping rule defines breakpoints corresponding to the user-definable number of groups. Application of the rule the

data divides the data into groups based on the breakpoints. The method may include presenting the grouped data in a manner that visually distinguishes the groups. In some embodiments, the grouping rules associate colors with groups and the grouped data is presented with an aspect of the data colored according to the rules.

Sometimes the data are in labeled columns in a spreadsheet, and the grouping rule specifies at least one breakpoint and a corresponding color for each range defined by the breakpoint. The grouped data are presented by coloring each data item in one labeled column of the data based on the breakpoint and the corresponding color of the breakpoint.

The breakpoints may be numeric or textual values. In some embodiments, the breakpoint is determined automatically based on the data.

Sometimes the data are provided in a table, and backgrounds of table cells are colored according to the rules.

The number of groups may be fewer than a number of possible data values.

In another aspect, this invention is a method of operating on data by providing at least one user-defined grouping rule for grouping the data into a user-definable number of groups. The grouping rule is applied to the data to generate grouped data. At least one user-defined scoring rule is used to score grouped data according to user-defined scores. The scoring rule is applied to the grouped data to score the grouped data.

In yet another aspect, this invention is a method of operating on data, in which data are grouped by applying to the data at least one user-defined grouping rule for grouping the data into a user-definable number of groups. The grouped

data are scored by applying to the grouped data at least one user-defined scoring rule for scoring the grouped data according to user-defined scores.

In some embodiments the data can be a number of parameters for each of a number of cases and the scoring rule comprises a scoring function of user-selectable parameters and user-defined weights for the selected parameters to be used in scoring the cases. The scoring applies the function to the data to obtain a score for each case. Sometimes the method includes sorting the scored cases by score, individually or by cluster, as described below.

The notion of clustering is that subsets of the various cases may be associated into clusters by having identical entries in any user-selected column of data, known as a clustering column. In some embodiments of the invention, the integrated clusters are treated by averaging the properties of all the cases which comprise each cluster.

Thus, according to aspects of this invention, in order to facilitate analysis and pattern recognition in large, multidimensional data sets, the precision of the data is potentially changed (implemented, e.g., by grouping the data) and then the data are presented for visualization (implemented, e.g., by coloring the data).

Brief Description of the Drawings

This file contains at least one drawing executed in color. Copies of this patent with color drawings will be provided by the United States Patent and Trademark Office upon request and payment of the necessary fee.

The above and other objects and advantages of the invention will be apparent upon consideration of the following detailed description, taken in

conjunction with the accompanying drawings, in which the reference characters refer to like parts throughout and in which:

FIGURE 1 shows a typical computer system on which the present invention operates;

FIGURE 2 shows an overview of the functionality of the present invention;

FIGURES 3A-3B depict a display of data in a spreadsheet;

FIGURES 4A-4B show a color control rules worksheet according to one embodiment of the present invention;

FIGURES 5A-5B show data coloring rules;

FIGURES 6A-6C show a data coloring control panel and a flow chart of the data coloring process, respectively;

FIGURES 7A-8B show the worksheet of **FIGURE 3A** and **3B** after various coloring rules in **FIGURE 4A** have been applied;

FIGURES 9A, 9B, 10A, and **10B** depict displays of data in spreadsheets;

FIGURES 11A and **11B** show the form of the cluster control worksheet according to one embodiment of the present invention;

FIGURES 11C-11D shows control panels from the cluster control worksheet of **FIGURES 11A-11B**;

FIGURE 12 shows the enlarging of the cluster starts mechanism according to one embodiment of the present invention;

FIGURES 13A-13D show the application of vertical display re-scaling according to one embodiment of the present invention;

FIGURES 14A-14D and **15A-15B** show the application of the scoring and sorting of clusters according to one embodiment of the present invention;

FIGURES 16A-16N, 16P and **16Q** show aspects of the application of the dose-response scoring and estimation of potencies according to one embodiment of the present invention;

FIGURES 17A-17B show the application of the sheet statistics tool according to one embodiment of the present invention;

FIGURES 18A-18D show the application of the scoring and sorting of clusters for the purpose of project prioritization and management according to one embodiment of the present invention;

FIGURES 19-24 show examples of the application of this invention to various types of data; and

FIGURES 25 and **26** show application of an aspect of this invention.

DETAILED DESCRIPTION OF THE PRESENTLY PREFERRED EXEMPLARY EMBODIMENTS

Overview

FIGURE 1 shows a typical computer system **100** on which the present invention operates. The computer system **100** includes a processor (CPU) **102** connected to a memory system **104** and a display **106**. The computer system also includes various input devices including a keyboard **108** and a mouse **110** or other pointing device. Internal storage **112** (e.g., a hard disk, a CD ROM and the like) and external storage **114** (such as a floppy disk, CD ROM and the like) are also provided.

Various aspects of this invention are implemented as computer software programs or algorithms **116** which run on the computer system **100**. The software programs **116** can reside in the internal storage **112**, the external storage **114**,

and/or in the memory **104**. The software programs **116** operate on data **118** which is provided, e.g., on the external storage **114**. The software programs **116** operate in a standard and known manner by being executed on the processor **102** of the computer system **100**.

In some embodiments of the present invention, the user can create and modify various executable rules **120** which can operate on the data **118**. For the sake only of explanation, the rules **120** are depicted separately from the data in the figures. However, as explained in more detail below, some or all of the rules **120** can be part of the data **118**.

In preferred embodiments, the computer system **100** is capable of running the spreadsheet program EXCEL™ 95 (hereinafter "EXCEL") from Microsoft Corporation, and the software computer programs **116** are written in Microsoft Corporation's Visual Basic (hereinafter "VB") and are provided as an add-in to EXCEL. A single copy of software thus serves all data files on a particular machine. To conserve EXCEL resources, in some embodiments, the package self-installs the add-in when the user opens a data file, and un-installs the add-in when the last data file in memory is closed.

In a preferred embodiment, this invention works entirely within the environment of EXCEL. EXCEL structures data files as workbook files which contain worksheets. The programs **116** of this invention consist of special EXCEL worksheets, called control sheets, on which input data is written by the user into designated labeled cells. The control sheets are part of the same EXCEL workbook file as the data. The control sheets also contain action buttons to execute the various procedures associated with this invention. The rules **120** are formed by setting various parameters in the control sheets.

When the workbook file is saved, the parameters (for the rules **120**) are stored on the control sheets along with the data, and they can be modified and/or re-executed at any time without having to re-enter anything. The results of operations are automatically written as worksheets in the same workbook file, providing a convenient, integrated data environment in a single file.

The system according to the present invention operates, in one aspect, in accordance with **FIGURE 2**. Recall that the user's aim is to perform analysis and pattern recognition in large, multidimensional data sets using (potentially low resolution) data grouping. To this end, the user and/or the system will create rules for coloring and presenting the data. First (at **122**) a user creates and organizes the data **118**. Various tools (discussed below) are provided to aid in the creation and organization of the data. Then (at **124**) the user creates rules **120** for operating on the data **118**. The rules **120** can be created before or after the data **118**, rules can be reused for different sets of data and multiple rules can apply to the same data. The creation and operation of rules are discussed in greater detail below. Once the data **118** and the rules **120** are created, the user then selects some (or all) of the rules to apply to the data (at **126**). Specifically, the user groups and thereby colors the data according to selected rules. With the data grouped and colored according to the rules, the user can then perform group/color-mediated data mining (at **128**).

FIGURES 3A-3B show views of the program of this invention in operation with a sample EXCEL sheet **300**, denoted "DEMO 1" (**302**) containing data (not all the data in the sheet is visible). The views of EXCEL worksheets shown in the various figures and examples that follow are the views that are presented on the display **106** of the computer system **100**. Sheets in an EXCEL workbook are labeled with tabs at the bottom of the worksheet. The data on the "DEMO1" sheet

300 consists of eight columns of data for each of a number of compounds. The compounds are denoted "Cmpd*xx*", where "*xx*" ranges from "01" to the number of compounds. In **FIGURE 3B**, the last compound visible on the data sheet is "Cmpd58". The eight columns are headed:

1. "Cmpd" (column A);
2. "Series" (column B);
3. "Test1" (column C);
4. "Test2" (column D);
5. "Test3" (column E);
6. "HTS SPA Dose-Resp % Inhib @3x10-6M" (column F);
7. "HTS SPA Dose-Resp % Inhib @ 1x10-6M" (column G);
8. "HTS SPA Dose-Resp % Inhib @ 3x10-7M" (column H); and
9. "HTS SPA Dose-Resp % Inhib @ 1x10-7M" (column I).

In addition to the "DEMO 1" worksheet **300**, the EXCEL workbook shown in **FIGURES 3A** and **3B** has seven other worksheets, denoted "DEMO 2" **304**; "DEMO 3" **306**; "clusterinfo DEMO" **308**; "Append Control" **310**; "Color Control" **312** and "Cluster Control" **314**. The last three worksheets, denoted respectively "Append Control"; "Color Control" and "Cluster Control," contain various rules and controls (to be discussed below). The data in worksheets denoted "DEMO 1" **302**; "DEMO 2" **304**; "DEMO 3" **306**; and "clusterinfo DEMO" **308** correspond to data **118** (**FIGURE 1**) and the controls or rules in the worksheets denoted "Append Control" **310**; "Color Control" **312**, and "Cluster Control" correspond to the rules **120** (**FIGURE 1**).

FIGURES 4A-4B show a color control rules worksheet (**312**, denoted "color control") according to the present invention, as displayed on display **106** of the

computer system **100**. The color control worksheet **312** is shown with some rules already in place, i.e., having values set, and other rules left blank. These rules are shown as examples only, and, as with any of the other types of rules, any or all of the rules can be set by the user. A typical data coloring rule **130** is shown in **FIGURE 5A**. The rule **130** has already been set up and operates on the appropriate data when selected by a user (using mouse **110**, **FIGURE 1** or some other pointing device) in the area **132** marked "Click here to run these". The rule **130** (as with all of the preferred color control rules) has four parts, namely the name of the sheet **134** containing the data on which the rule is to operate ("DEMO 1" in the example of **FIGURE 5A**); the columns **136** of data of the sheet on which the rule is to operate ("E" in the example of **FIGURE 5A**); the number of colors **138** to be used by the rule **130**; a number of breakpoints **140** (denoted "break 1" to "break 4" in the example of **FIGURE 5A**); and a corresponding number of colors **142** for each range defined by the breakpoints (denoted "color 1" to color 4" in the example of **FIGURE 5A**). Actually, as explained below, the number of breakpoints is one less than the number of colors.. In the specific example shown in **FIGURE 5A**, the rule has three breakpoints of 1, 5 and 10, defining four ranges with four corresponding colors **142**, namely light green, yellow, orange and red. Preferably the named colors are also depicted in the actual colors, so that, in this example, the background of the word "lightgreen" is shown in light green, the background of the word "yellow" is shown in yellow and so on.

In this invention it is preferable to show data and meta-data (headings etc.) in color. In some embodiments, the coloring is implemented by showing a background area of the text representing the data in the appropriate color. Sometimes the actual text representing the data is shown in the appropriate color.

In presently preferred embodiments, the font color is only changed in cases where necessary to improve contrast with the background color for readability. Only two font colors, dark (black) and light (pale gray), are used in the presently preferred embodiment. Combinations of both approaches can be used. For example, the background section of the word "yellow" is preferably shown in the color yellow. It is also possible to show the word itself, i.e., the font, in the color yellow, as long as that color is distinguishable from the background.

The particular rule **130** shown in **FIGURES 4A** and **5A**, operates as follows, when selected:

In sheet "DEMO 1" **302**, in column E, values less than or equal to 1 (break 1) are colored light green (color 1); values in the range 1 to 5 (between break 1 and break 2) are colored yellow (color 2); values in the range 5 to 10 (break 2 to break 3) are colored orange (color 3); and values greater than 10 (break 3) are colored red (color 4).

Another typical data coloring rule **130-1** from the color control sheet **312** is shown in **FIGURE 5B**. The rule **130-1** is set up to operate on columns "C" and "D" of sheet "DEMO 1". The rule **130-1** uses three (3) breakpoints (break1=0.1, break2=1 and break3=5) defining four ranges with four (4) corresponding colors ("lightgreen", "yellow", "orange", and "red").

The results of applying the rule **130-1** of **FIGURE 5B** to the data in sheet "DEMO 1" (302, **FIGURE 3**) are shown in **FIGURES 7A-7B**. As can be seen from **FIGURES 7A-7B**, after application of the rule **130-1**, all of the data in columns C and D of the sheet labeled "DEMO 1" has been colored according to the rule. Specifically, data having a value less than or equal to break 1 (0.1) have been colored light green; data values in the range between break 1 and break 2 (0.1 to

1) have been colored yellow; data values in the range between break 2 and break 3 (1 to 5) have been colored orange; and data values greater than break 3 (5) have been colored red.

The results of applying all of the other color control rules shown in **FIGURES 4A-4B** to the data in sheet "DEMO 1" are shown in **FIGURES 8A-8B**. The rules can be applied individually (as shown above with respect to **FIGURES 7A-7B**), or they can be all be applied at the same time. In order to apply all rules to a particular data set (sheet), each rule can be individually selected or the area labeled "RE-RUN ALL RULES FOR SHEET NAMED DEMO 1" (on the right side of **FIGURE 4A**) can be selected. Note that if two rules apply to the same column of the same sheet, the second rule run on that column will override the first rule run on that column.

To create a coloring rule a user performs the following (with reference to **FIGURE 6B**):

(1) Select the "COLOR CONTROL" sheet **312** and pick a control panel on that sheet to use (an empty panel or one containing a rule no longer needed) (at **600**). All control panels on a sheet can be cleared by clicking the button labeled "CLEAR ALL ENTRIES ON THIS SHEET" (**318** in **FIGURE 4A**).

(2) In the selected control panel, enter the name of the sheet to be colored (at **602**).

(3) In the selected control panel, enter a column or columns (at **604**). For multiple columns, either list them separated by commas, or use a colon or hyphen to denote ranges, or some combination. For example, "A:D,F" means columns A,B,C,D, and F. To aid in

choosing columns, the user can right-click on the cell containing the name of the data sheet, and pick "Open Twin Screen" from the shortcut menu that appears, to create a special dual display. This also creates a "Close Twin Screen" button to go back.

(4) Choose a number of colors to use (at **606**), either by entering the number of colors or by repeatedly clicking the gray button adjacent the cell labeled "# of colors". In preferred embodiments, the system allows for five breakpoints and six colors per rule. Accordingly, the numbers will cycle from 1 to 6, and various cells below them will be blacked out accordingly.

(5) Enter the breakpoints that define the color groups (at **608**), in any of three modes:

a) *Numeric data, manual mode*: enter numbers to form the breakpoints, i.e., the boundaries between the color groups, one less than the number of colors, in increasing numerical order. Cells whose values exactly equal a breakpoint value will be colored with the lower group (breakpoint 1 is colored with color 1, etc.)

b) *Numeric data, automatic mode*: enter either "value", "log", or "count" as the first breakpoint. If multiple columns have been chosen, the user must also enter "yes" or "no" opposite "Re-scale all?" at the bottom of the panel, to indicate whether each column should get its own auto-breakpoints, or whether the

auto-breakpoints of the first column (first in list in the rule, not first on the data sheet) should be used for all.

This mode reports information about the breakpoints it determines, and thus could also be used to explore the distribution of numerical values in a column prior to a final *manual* breakpoint selection.

c) Text data: enter the strings to be matched and colored, in preferred embodiments, up to five (5) in number. Matching is case-insensitive unless the string is enclosed in double quotes (“ and ”); otherwise, no quotation marks are necessary.

Several special text strings act as operators if entered as the first word in a rule cell:

Rule Entry (OPERATORS need not be uppercase—here only for emphasis)	**Meaning**
test string	color data cell if its whole content matches the test string
NOT test string	• color data cell if its whole content does not match the test string; • will not color numeric cells
CONTAINS test string	color data cell if contains the test string as a substring anywhere
NOTCONTAINS test string	• color data cell if it does not contain the test string anywhere; • will not color numeric cells

Rule Entry (OPERATORS need not be uppercase—here only for emphasis)	**Meaning**
BEGINS test string	color data cell if it begins with the test string
ENDS test string	color data cell if it ends with the test string
* (an asterisk)	(wildcard) color data cell containing any data, including numeric cells
BLANK	color data cells that are blank

Using quotes to force matching to be case-sensitive also works with strings that follow an operator.

It is possible to construct a text-coloring rule in which certain cells may satisfy more than one of the "breakpoint" values. For example, if a rule says that "active" is colored green and "contains act" is colored red, then the word "active" in a cell would satisfy both. In such cases, the system colors the cell according to the *first* condition satisfied on the list of breakpoints. This dependence on the order can be used advantageously to achieve complex coloring conditions. The sequence of conditions can be considered as a series of filters, through which only the as-yet-uncolored cells fall through to the next decision.

(6) Enter the names of the colors to use (at **610**), in the order corresponding to the breakpoints. A display of color samples is provided at the right side of the Color Control sheet **312**. A user need only enter the name, and the appropriate cell will become colored when the tool is executed. If the user wants the color to display immediately, he can copy and paste the sample cell into the rule's color cell. A special pseudo-color named "SKIP" is used to tell the system not to color the cells whose data falls in this group.

(7) When the rule has been created, the user executes the rule by selecting the rule's "CLICK HERE TO RUN THESE" button on the panel filled in (at **612, FIGURE 6C**).

(8) To create different coloring rules for other columns, repeat the above in additional control panels. If the user runs out of control panels, he can create more control panels by copying an existing one and pasting it onto a blank section of the color control sheet.

To the extent that a single panel cannot hold all the requirements for a particular rule, a user can combine two or more panels to create a particular rule. For example, if a user needs ten (10) breakpoints, two panels can be used.

With reference to the coloring rule is shown in **FIGURE 6A**, once the rule has been set, a number of parameters are stored in the system. The parameters are "sheet name" ("DEMO 3" in **FIGURE 6A**), column specification, number of colors, array of breakpoints, array of colors, and multicolumn scaling mode.

The data coloring mechanism operates as follows, with reference to the flowchart of **FIGURE 6C**.:

1. The user enters the parameters into a rule panel on a "COLOR CONTROL" worksheet **312**, e.g., as described above with reference to the panel of **FIGURE 6A**.

2. The user selects (clicks) the activation button (labeled "Click here to run these") on that panel (at **612**). This causes the system to:

(A) Read and interpret the parameters from the panel (at **614**). The system can identify which button was clicked using the Visual Basic ("VB") "caller" property, described in more detail below. The parameters are then read based on the identity of the cell location of the button using the VB "TopLeftCell" property. The system retrieves the parameters (sheet name, column specification, number of colors, array of breakpoints, array of colors, and multicolumn scaling mode) from cells in this panel by relative reference to the button cell.

(B) Next, determine the mode of the coloring rule (at **616**) (i.e., numeric v. text or manual v. automatic, and, if automatic, which of value, log or count). This uses the analysis of the first breakpoint entry.

(C) Compile a list of the columns specified in the "column specification" parameter (at **618**). This is done by scanning the various areas contained in the selection, as follows:

```
For Each singlearea In Selection.Areas
     For Each c In singlearea.Columns
          If Not CountEmpty Then
               lr = LastRowInColumn(c.Column)
          End If
```

```
            If Not CountEmpty And lr = 0 Then
                    'skip this empty column
                ncols = ncols - 1
            Else            ' add this column to the list
                icol = icol + 1
                colnumarray(icol) = c.Column
            End If
        Next c
    Next singlearea
```

(D) If an auto-breakpoint mode is being used (determined at **620**), analyze the data values to determine the breakpoints (at **622**). This is done by:

(i) Collecting statistics on the data distribution in each specified column; and

(ii) Calculating the automatic break points for the appropriate mode. For example, the auto-value breakpoints are determined as follows:

```
If breakmode = "VALUE" Then
    interval = (maxvalue - minvalue) / ncolors
    break(0) = minvalue
    For ibreak = 1 To ncolors - 1
        break(ibreak) = break(ibreak - 1) + interval
    Next ibreak
```

(iii) Displaying the results for user approval or cancellation.

(C) Loop through the cells in the chosen columns on the chosen worksheet (at **624**).

(D) Compare each cell's value to the list of breakpoints (at **626**). If the coloring rule is in text mode, use the meanings of the special breakpoint operators ("contains", "blank", asterisk "*"; or quotation marks).

(E) When a match is found, apply the appropriate color (at **628**).

The code below illustrates the processes (D) and (E) for numeric breakpoints:

```
For Each cell In Range(Cells(StartColoringRow, colnum),
                       Cells(FinishColoringRow, colnum))
      cvalue = cell.Value
      colored = False
      If IsNumeric(cell.Value) Then
            If Not IsEmpty(cell) Then
            ' (have to test both because EMPTY is numeric)
                  For ibreak = 1 To ncolors - 1
                        If cvalue <= break(ibreak) Then
                        If Color(ibreak) <> "SKIP"
                              cell.Interior.ColorIndex =
                               Color(ibreak)
                              Call TextContrast(cell)
                        End If
                        colored = True
                  Exit For
                  End If
                  Next ibreak
      If colored = False Then
            ' Not hit yet?  Must be top category, so:
            If Color(ncolors) <> "SKIP"
                  cell.Interior.ColorIndex = Color(ncolors)
                  Call TextContrast(cell)
```

```
                End If
                colored = True
            End If
            End If
            Else     ' not numeric - just don't color it
    End If
    Next cell
```

The operation of the data coloring tool of this invention will now be described in greater detail. Each coloring rule is provided in a coloring control panel that has the general form of a coloring rule as shown in **FIGURE 6A**. In one preferred embodiment, each coloring control panel **144** is a double-outlined unit, sixteen (16) cells high by two (2) cells wide. As noted above, a user is provided with coloring control panels on the color control worksheet **312**. A user can use the coloring control panel **144** to set the sheet and column(s) on which the rule is to operate, the number of colors, the various break points and the colors associated with those breakpoints. The sheet is set by entering its name into the cell **146** adjacent the cell labeled “sheet”. The column (or columns) on which the rule is to operate is (are) set by entering its (their) name in the cell **148** adjacent the cell labeled “column(s)”. The number of colors is set by the user by selecting the cell **150** adjacent to the cell labeled “# of colors”. Each time the cell **150** is selected it increases the number of colors, up to a maximum of six (6), i.e., rotating through the values 1 to 6. I.e., when the cell **150** shows a “6” and is selected, it reverts back to “1”. That is, selecting the cell **150** causes the value in the cell to cycle from “1” to “6” and then back to “1”.

A Visual Basic (“VB”) macro function (“*CallColorColumn*”) is associated with the top cell **152** of the control panel **144**. When the cell **152** is selected by

the user (with the mouse **110** or the like), the function associated with that cell is executed by the computer (CPU **102**). In the presently preferred embodiments, the *CallColorColumn* function extracts the button name of the cell **152** and then calls a second function ("*CallColorColumnSubroutine*") with that button name as one of the parameters. The function *CallColorColumnSubroutine* takes three parameters, namely *ButtonName*, *StartColoringRow*, and *FinishColoringRow*. The two parameters *StartColoringRow*, and *FinishColoringRow* are optional.

First, the function *CallColorColumnSubroutine* determines what specific values to use for the coloring by reading them from the control panel **144**. Since the values are all in fixed positions relative to the selected button cell **152** that initiated the call to the function *CallColorColumn*, the values can be determined once the location of that button cell **152** has been determined. This is done using the following Visual Basic code:

```
Sheets("Color Control").Activate
headingrow =
     ActiveSheet.Buttons(ButtonName).TopLeftCell.Row
headingcol =

ActiveSheet.Buttons(ButtonName).TopLeftCell.Column
```

Note that if the function *CallColorColumnSubroutine* was called from another sheet (not "Color Control") then this method will not find it.

The various parameter values are then read as follows:

Sheet name:

```
datacol = headingcol + 1
sheetname = Trim(Cells(headingrow + 1, datacol).Value)
```

If there is no sheet named "sheetname" an error function is called. Generally, in preferred embodiments, a great deal of error checking takes place to ensure that the user is provided with a friendly and useable interface to the program. Most of the error checking is not mentioned in this description, however, one skilled in the art would know what kinds of error checking to implement in order to provide a user-friendly working environment.

The column(s) to be colored are specified by:

```
Cells(headingrow + 2, datacol).Value
```

The number of colors is specified by the variable *ncolors*, where:

```
ncolors = Cells(headingrow + 3, datacol).Value
```

Within the function *CallColorColumnSubroutine* there are two arrays, named *break* and *color*, which are used to store the breakpoints and colors, respectively. The first breakpoint is set as follows:

```
break(1) = Cells(headingrow + 4, datacol).Value
```

The value of the first breakpoint is used to determine the break mode ("NUMERIC", "VALUE", "LOG", or "COUNT"). If *break(1)* (as determined above) is numeric, then the mode is set to "NUMERIC", otherwise, if *break(1)* is one of "VALUE", "LOG", or "COUNT", then the break mode is set to that mode, otherwise the break mode is set to "TEXT".

Next, the function determines whether multiple columns were specified, in which case it determines whether the user selected to re-scale all the columns. The user's re-scale selection is determined by:

```
rescale_all_string = Cells(headingrow +
15,datacol).Value
```

Now the rest of the breakpoints (if any) are read. If the break-mode is "AUTO" then the breakpoints are set as follows:

```
For i = 2 To lastbreaknum
    break(i) = Cells(headingrow + 3 + i, datacol).Value
```

Various possible errors are checked for. E.g., if any breakpoints are missing (i.e., if *break(I) is empty,* the user is notified. Also, if the break mode is "NUMERIC" and non-numeric breakpoints are set, the user is notified. If numeric breakpoints are not in increasing order, the user is notified. As noted above, generally, in preferred embodiments of the present invention, a great deal of error checking is performed on all user inputs to ensure that the values are correct and consistent. Most error checking is omitted from this description.

The *CallColorColumnSubroutine* maintains an array, *colorname,* which maps integers to colors. In preferred embodiments, there are fifty six (56) colors available. To use the higher numbered colors, the computer's video card must be set appropriately. Using the *colorname* array, the program next associates the user provided color names with index numbers. Specifically, for each of the (up to six in a preferred embodiment) colors specified, the user specifies an actual color name, denoted *cname*. This name is determined for each color by:

```
For j = 1 To ncolors
    cname = Cells(headingrow + 8 + j, datacol).Value
```

The interior of each color-specifying cell is then colored by the appropriate (selected) color by setting the color property (*Interior.ColorIndex*) of the cell:

```
Cells(headingrow + 8 + j, datacol).Interior.ColorIndex =
        Color(j),
```

where the value of the variable *j* ranges from 1 to *ncolors*.

Then the cell is further processed by a function *TextContrast*.

```
        Call TextContrast(Cells(headingrow + 8 + j, datacol))
```

With the parameters read and checked, the system is ready to process and color the selected sheet (specified at cell **146** in **FIGURE 6A**). The selected columns (specified in cell **148** in **FIGURE 6A**) in the selected sheet are processed one-by-one by the following program code:

```
Call ParseInput(InString, inspecifier)
For Each singlearea In Range(inspecifier).Areas
        For Each c In singlearea.Columns
                colnum = c.Column
                Call ProcessOneColumn(colnum, ncolors, break,
                                        Color, breakmode,
                                        rescale_all, sheetname,
                                        StartColoringRow,
                                        FinishColoringRow)
        Next c
Next singlearea
```

The processing performed by the function *ProcessOneColumn* is as follows: The column designated by *colnum* on sheet *sheetname* is to be colored according to the breakpoints in the array *break* and the colors in the array *colors*. The designated column is colored from the row corresponding to *StartColoringRow* to the row corresponding to *FinishColoringRow*. Note that the

function *ProcessOneColumn* is also provided with the break mode and the variable *rescale_all*.

Function *ProcessOneColumn* first calculates the automatic breakpoints, if necessary. Note that automatic breakpoints are determined from the whole column, even if this call says to color only a limited range of rows. If the value of *breakmode* is "VALUE" or "LOG" and the value of *rescale_all* is set to “True” Or the value of the first breakpoint (*break(1)*) is set to "VALUE" or "LOG", the program calls the function *AutoValueBreakpoints* as follows:

```
Call AutoValueBreakpoints(colnum, colletter, ncolors,
break, Color, breakmode, rescale_all).
```

Otherwise, if the *breakmode* is set to "COUNT" and the value of *rescale_all* is set to “True” or the first breakpoint (*break(1)*) is set to "COUNT", then the program calls the function *AutoCountBreakpoints*, as follows:

```
Call AutoCountBreakpoints (colnum, colletter, ncolors,
break, Color, breakmode, rescale_all, sheetname).
```

With the breakpoints calculated, the columns are colored according to the type of breakpoints specified by the user. Specifically, when the *breakmode* is any one of "VALUE", "COUNT", "LOG", or "NUMERIC", the system executes a function *ColorNumericColumn*. On the other hand, when the *breakmode* is “TEXT”, the system executes a function *ColorNumericColumn*. The VB code for this is as follows:

```
Select Case breakmode
    Case "VALUE", "COUNT", "LOG", "NUMERIC"
```

```
            Call ColorNumericColumn(colletter, ncolors,
break, Color, StartColoringRow, FinishColoringRow)
        Case "TEXT"
            Call ColorTextColumn(colletter, ncolors, break,
Color, StartColoringRow, FinishColoringRow)
End Select
```

Then, when the rule in control panel **144** is selected for execution, the rule is applied to the selected column(s) (denoted in cell **148**) of the named sheet (in cell **146**). For each column in the named sheet, the value in each cell is compared to the various breakpoints and the cell is colored corresponding to the appropriate breakpoint.

Examples of the application of various coloring rules in the "COLOR CONTROL" worksheet of **FIGURES 4A-4B**, are shown with reference to the data in worksheet "DEMO 2" (depicted in **FIGURES 9A, 9B, 10A** and **10B**).

<u>Color-Mediated Data Mining</u>

As noted above with reference to **FIGURE 2**, once the data have been colored according to the user-selected rules (at **126**), the user can then perform color-mediated data mining (at **128**). The presently preferred embodiment of this invention provides five mechanisms (each discussed below) for color-mediated data mining, namely mechanisms to:

1. enlarge/shrink cluster starts;
2. vertically re-scale the display;
3. score and sort clusters; and
4. score and sort dose-response data.

The following discussion refers to the cluster control worksheet which is shown in **FIGURES 11A-11B**.

1. Enlarge/Shrink Cluster Starts

The "Enlarge Cluster Starts" mechanism highlights the first row of each cluster in clustered data by enlarging the font of the cell containing the cluster number or label, thus enabling size reduction of the spreadsheet for the user to focus on the color patterns. When the cell height is dramatically reduced in order to see more cells on a screen or printed page, this enlargement allows the user to still read the label at the beginning of each cluster. The mechanism takes user input from a *Cluster Control* worksheet. A corresponding mechanism ("SHRINK CLUSTER STARTS") allows for undoing the enlarging. This mechanism handles cluster numbers or textual labels. Any column can be designated as the cluster labels to be processed.

Operation of the mechanism is as follows:

(1) From the "CLUSTER CONTROL" sheet **314** pick a control panel to use (one which is empty or one containing inputs no longer needed). On this sheet, a single control panel extends vertically through the black, blue, red, and green sections, and provides input information for several tools.

(2) In the blue section, enter a sheet name and the column to be considered as the cluster labels.

(3) Click either the blue-text "Enlarge Cluster Starts" or "Shrink Cluster Starts" button.

The program code accomplishes this by scanning the column of cluster labels, identifying any entries that are different from the one immediately above, and enlarging them. Code that carries out this function is shown below:

```
For Each c In Range(Cells(3, colnum), Cells(lastrow,
colnum))
      irow = c.Row - 1
      icol = c.Column
      If c.Value <> Cells(irow, icol).Value Then
            c.Font.Size = bigfontsize
      '          Rows(Irow + 1).RowHeight = bigrowheight
      End If
Next c
```

Example

An example of the application of the enlarge cluster mechanism is shown in **FIGURE 12** which shows the application of a rule (shown in the control panel **FIGURE 11C**) from the cluster control worksheet in **FIGURE 11B** to the data of worksheet "DEMO 2" as shown after coloring in **FIGURES 10A-10B**. As shown in **FIGURE 11C**, the rule is to be applied to column B of sheet "DEMO 2".

2. Vertical Display Re-Scaling

The vertical re-scaling mechanism operates by taking a user-provided scale factor and then changing height of data rows to facilitate visualization of large-scale color patterns. The mechanism leaves column heading heights and column widths unchanged. This makes headings remain readable and greatly simplifies examining long columns of data for color patterns.

FIGURES 13A-13D show the application of the vertical display re-scale mechanism according to the present invention. FIGURES 13A-13B show some of the data in the worksheet labeled "DEMO 3" 306 (FIGURE 13A shows the first thirty eight or so elements and FIGURE 13B shows the remaining elements of that worksheet). As can be seen from the figures, the worksheet "DEMO 3" 306 has three hundred and twenty eight (328) data entries (in rows 2-329). The user can vertically scale the display by selecting "Re-scale Vertical" from the system's special menu or by pressing a particular control key sequence (e.g., "CNTL-SHIFT-V" in a preferred embodiment). This presents the user with a dialog box 318, as shown in FIGURE 13C, which asks the user to enter a scaling factor relative to the current size. The user enters a scaling factor to enlarge or reduce or restore the display. In the example shown, the user enters a scaling factor of 0.1 which produces the vertically scaled display shown in FIGURE 13D.

Vertical scaling allows a user to get an overview of the data, based on the coloring.

The portion of the program code presented below carries out the central function of the vertical display rescaling mechanism:

```
rowspec = "2:" & lastrow ' leaves the headings unchanged,
i.e., readable
If factor = -1 Then
      Rows(rowspec).Rows.AutoFit
Else
      For irow = 2 To lastrow
            Rows(irow).RowHeight =
                     Rows(irow).RowHeight * factor
      Next irow
End If
```

After execution of the rescaling mechanism, as can be seen in FIGURE **13D**, the height of each row (except the heading rows) has been scaled by *factor*, 0.1 in the example shown. In this manner, all rows of the data are made visible on a single page, thereby facilitating data analysis.

3. Scoring and Sorting Clusters

Scoring and sorting clusters assign numerical scores to the color patterns of individual rows or clusters of rows, thereby enabling comparison and sorting of the clusters by score.

The scoring and sorting mechanism accepts user's designations of colors and corresponding relative scores. It handles cluster numbers or textual labels. Any column can be designated as the cluster labels to be processed. The mechanism scores a user-selected list of columns of data, with user-assigned relative weights, which need not be equal for all columns.

User input is taken from a *Cluster Control* worksheet **314** (see FIGURES **11A** and **11B**), which stores any number of parameter sets, each one with a user-specified name.

The input data is automatically sorted by cluster label before starting, in order to group the clusters together in case the user has previously sorted the data by some other criterion. Then scores are normalized to remove the effects of cluster size, absolute magnitude of scoring points chosen, and absolute size of weights chosen. The results are written to two new worksheets without altering the original data sheet. The first derived sheet is for the numerical scores; the second is like the original, but has the clusters sorted into descending score order,

so that the "best" are at the top, removing the need to visually scan a long colored worksheet. The derived output sheets have names that indicate their source data sheet and the name of the parameter set used for scoring. At the user's option, the system reversibly hides the un-scored columns in the cluster-sorted output sheet, focusing attention on the data that were used in scoring.

In preferred embodiments, the system detects uncolored cells in the data and offers the user two programmed modes of dealing with them, (uncolored = entry on user's list of scores or uncolored = "average of other colors in row"), or the option of stopping to color them manually.

If the user designates a column of individual compound labels as the "cluster labels," then the system compares single compounds rather than clusters.

The mechanism operates as follows, with reference to **FIGURES 11A-11C**.

(1) On the "Cluster Control" sheet **314** the user picks a control panel (e.g., panel **1100**) to use (a panel which is empty or one containing non-needed inputs). On this sheet, a single control panel extends vertically through the black, blue, red, and green sections, and provides input information for several tools.

(2) In the top black section **1102** of the selected control panel **1100**, the user gives this new parameter set a name if not already done. The name will be used to label the outputs.

(3) In the blue section, the user enters a sheet name (in **1104**) and the column (in **1106**) to be considered as the cluster labels. Note: To score each compound separately rather than in clusters, enter a column with individual compound labels as the "Cluster Col."

(4) The red section of the contro panel is divided into two parts, with its action button **1108**, with red text "Score and Sort Clusters", in the middle. Above the button, enter the names of the colors **1110** to be assigned point scores, along with their corresponding point scores **1112**. The scores are arbitrary and relative; they will be normalized by the system as necessary. However, a user should be sure always to assign higher point scores to colors which denote favorable values, and lower point scores to colors which denote unfavorable values. The cells with entries need not be colored, and need not be in score order, because the system will color and sort these cells when run.

When assigning point values, a user should be aware that uncolored cells (which are most likely blank, i.e., unknown data) may have quality values above or below those that contain grouped and colored data.. The user may decide that some of the colored groups are "better" or "worse" than data being unknown, and can assign a score to the color "NONE" accordingly.

(5) Below the "Score and Sort Cluster" button **1108**, the user enters the columns **1114** to use for scoring (using the same syntax as for the Data Coloring) and their corresponding relative weights **1116**. The numbers for weights are arbitrary and relative; they will be scaled by the system as necessary. Note that a line with multiple columns will assign the entered weight to *each* of the columns.

(6) The user the selects (clicks) the red-text "Score and Sort Clusters" button **1108**.

(7) When the scoring and sorting tool runs (on the system **100**), if the system detects uncolored cells in the data, the user will be offered two modes of dealing with them automatically, or a third manual option of stopping to color them. The two modes are:

- "Use score for the color "none" on my list" (RECOMMENDED)
- "uncolored = average of other colors in row".

(8) The program then scans the chosen columns in each row and adds up the chosen column's color scores for that row. These scores are then averaged for each cluster of rows, as defined by the user-selected "cluster column." The VB program code which accomplishes this is as follows:

```
For icol = 1 To ncols
      colorcode =
Cells(irow,colnum(icol)).Interior.ColorIndex
      colorfound = False
      ' Add up the weighted scores
      For j = 1 To ncolors
            If (icolor(j) = colorcode) Then
                  jscore = j
                  colorfound = True
                  Exit For
            End If
      Next j
      If colorcode = xlNone And treatblanks = "AVERAGED"
Then colorfound = True
      If Not colorfound Then
            Cells(irow, colnum(icol)).Select
      If colorcode = xlNone Then
```

```
            thiscname = "none"
        Else
            Call ColorNameToIndex(thiscname, colorcode, True)
        End If
        addscore = score(jscore) * colweight(icol)
        cmpdscore = cmpdscore + addscore
        ' Next IF-THEN-ELSE block is
        ' special calculations for the "averaged" mode
        If colorcode = xlNone Then
            lostweight = lostweight + colweight(icol)
            minscore = Application.Min(minscore, 0)
            maxscore = Application.Max(maxscore, 0)
        Else
            cmpdscore2 = cmpdscore2 + addscore
        End If
    Next icol
```

(9) The scores are then normalized for the various cluster sizes (number of rows per cluster), and scaled to a value of one hundred (100) for a row which is colored entirely with the user's highest-scoring color and a value of zero for a row that is colored entirely with any color to which the user has assigned a score of zero.

```
    If clusterscore(icluster) = 0 Then
        ' do nothing
    ElseIf clusterscore(icluster) > 0 Then
        clusterscore(icluster) =
            100 * clusterscore(icluster) / (nrows * maxscore)
    ElseIf clusterscore(icluster) < 0 Then
        clusterscore(icluster) =
            100 * clusterscore(icluster) /
                (nrows * (-minscore))
    End If
```

(10)The results are presented as two newly inserted worksheets. The first is named by appending the word "SCORES" to the name of the original data sheet, and contains a list of the clusters with their sizes and scores.

(11)The second new sheet is named by appending the word "SORTED" to the name of the original data sheet. The "SORTED" sheet contains a copy of all the original data and coloring, but with the rows re-ordered to place the highest-scoring clusters at the top, and all the clusters in descending score order from there down.

(12)The user has two additional options regarding the appearance of the "SORTED" sheet: (a) a column containing the numerical scores can be added; and (b) the columns that were not used in the scoring can be hidden, so that only the ones actually used remain visible.

An example of user provided data is shown in the control panel in **FIGURE 11D** which is taken from the cluster control worksheet shown in **FIGURE 11A**. As shown in **FIGURE 11A**, the parameters are stored with the name "Cmpd" **1102**. The scoring a sorting parameters in the control panel **1100** of **FIGURE 11D** give the color red a score of "-1", orange has a score of "0", yellow has a score of "1" and light green has a score of "2". Columns C and D have relative weights of "1", as does column E.

Note on the output of score and sort clusters: The system inserts two new sheets after the data (see, e.g., **FIGURES 14C-14D**). The first added sheet contains two score columns: the scores generated by *both* of the auto modes (uncolored = zero and uncolored = average), but the one not selected will be gray. The scores

are on a scale of "-100" to "+100", where a score of "-100" means that all cells had the maximally negative score available, and a score of "+100" means that all cells had the maximally positive score available. The second added sheet has clusters sorted according to the *one* auto mode chosen when the tool ran. The routine offers to hide all columns that were *not* used in the scoring and sorting. The user can selectively unhide certain columns by using the "Edit:GoTo" menu option (or typing "CTRL-G"), enter the columns in the "Reference" box (for example, C:F), then pick the "Format:Column:Unhide" menu option.

If the user wants to see a color-score-sorted list of compounds within a particular cluster (such as the best cluster), the user should do the following:

1. Sort by clusters to find the ID of the cluster wanted.
2. With a second rule, sort by compounds.
3. Go to the "SORTED by Compound" results sheet and turn on EXCEL's "Data:Filter:AutoFilter" feature for the column that specified the clustering in the first sort. The user can then choose to view only the compounds in one particular cluster, and they will be in compound-sorted order.

Example

With reference to the already-colored worksheet "DEMO 1" shown in **FIGURES 8A-8B**, the cluster control worksheet shown in **FIGURE 11A**, and the control panel shown in **FIGURE 11D**, application of the scoring and sorting of clusters is described. As noted above, in the control panel of **FIGURE 11D**, the parameters are stored with the name "Cmpd" **1102**. The color red has a score of

"-1", orange has a score of "0", yellow has a score of "1" and lightgreen has a score of "2". Columns C and D have relative weights of "1", as does column E.

Application of control panel "Cmpd" of **FIGURE 11D**, by selecting "Score and Sort Clusters", produces the worksheets shown in **FIGURES 14A-14B**. When the user selects the "Score and Sort Clusters" button **1108** for the "Cmpd" control panel of **FIGURE 11D**, the system first presents a dialog box (**1402** shown in **FIGURE 14A**) asking the user how un-colored cells should be scored for sorting. As noted above, un-colored cells can be scored explicitly by user entries (recommended) or as the average of the colors in the same row. Once the user makes a selection and clicks on the "OK" button, the system scores and sorts the data, producing the display screen shown in **FIGURE 14B**. The system provides a summary of what was done, including the information about the two new sheets ("DEMO 1 SCORES by Cmpd" and "DEMO 1 SORTED by Cmpd un=ze") which are added to the workbook. **FIGURES 14C-14D** show the data in the newly created worksheet "DEMO 1 SCORES by Cmpd".

<u>Example</u>

With reference to the already-colored worksheet "DEMO 2" shown in **FIGURES 10A-10B**, the cluster control worksheet shown in **FIGURE 11A**, and the control panel shown in **FIGURE 11C**, application of the scoring and sorting of clusters is described. In the control panel of **FIGURE 11C**, the parameters are stored with the name "acids" (**1102**). The color red has a score of "0", orange has a score of "1", yellow has a score of "2" and light green has a score of "3". Column D has a relative weight of "1".

The application of the parameters or rules in the "acids" control panel produces two new worksheets ("DEMO 2 SORTED by acids" and "DEMO 2 SCORES by acids") shown in **FIGURES 15A-15B**.

4. Score and Sort Dose-Response Data.

Data grouping and visualized by color coding has also been found to enable an automated solution to another vexing pattern recognition problem. An HTS lab is currently able to provide dose-response data on some subset of the whole collection of compounds originally tested. Sometimes, logistical constraints (time and/or cost) dictate that only a few concentration points can be run on each compound, and the high-throughput nature of the process generates somewhat noisy data. A similar situation sometimes exists in other biological laboratories where assays are very time-consuming. Dose-response curves with few, noisy points are difficult to analyze by traditional curve-fitting methods. The present invention includes a mechanisms/algorithms for analyzing percent-of-maximal-effect data and accurately ordering the compounds by potency, even when faced with few points and high noise.

The mechanism recognizes two properties of the dose-response data for each compound:

1. "Dose-responsiveness," the drop-off of activity with dilution, is taken as a sign that the compound has some reasonable pharmacological mechanism of action.

2. The activity measurements at the various concentrations also provide a confirmation of the general level of each compound's activity that was indicated by the original single-poke HTS hit.

These two properties are somewhat independent, as illustrated by the example of a compound that is 95% active at all tested concentrations. It demonstrates very poor (i.e., no) dose-responsiveness over the range of concentrations tested, but is so active that it should not be ignored, because it might reveal a dose response if tested at even lower concentrations.

By using the data groupings and color codes of the dose-dependent activity data columns, which help to smooth out excessively fine distinctions in the numbers, this invention includes an algorithm to assign numerical scores for dose-responsiveness and overall activity in the dose-response data. Moreover, the algorithm also calculates a smart composite of these two scores, in such a way that a highly active compound will get a high composite score even if its dose-responsiveness is poor. This composite score is capable of extracting useful information, even from very noisy data, and has been validated to correctly order a list of test compounds. The system of this invention adds data columns that report all three scores for each compound, and these columns can themselves be color coded, and thus used in further comparison to other types of data by compound or cluster scoring and sorting as described above.

Moreover, within certain limits, the invention's dose-response scoring algorithm can also be used to make *quantitative* estimates of IC_{50} values of compounds, even in the presence of large amounts of experimental error. This is accomplished by adding a set of hypothetical marker compounds with known potencies and theoretically calculated activities at the test concentrations. Since

the ordering algorithm is reliable, these markers will be ordered into their appropriate place, and can be used to calibrate the ordering scores in terms of actual IC_{50}'s. In other words, estimates of IC_{50} for the compounds can be generated by interpolating between the markers in the ordered list of composite scores.

Scoring and sorting dose-response data according to the present invention processes several columns of colored dose-response data (activity vs. concentration) to assign three numerical scores that can later also be color coded, and thus used by the "Score and Sort Clusters" mechanism (described above) to compare compounds or clusters of compounds. The three scores are:

(a) degree of dose-responsiveness over the concentration range tested;

(b) overall activity level demonstrated in the dose-response data; and

(c) a variably weighted composite of (a) and (b), designed to give high scores for high activity even when dose-responsiveness is poor (e.g., a compound that is highly active at all concentrations).

The scoring and sorting dose-response data according to the present invention bases its scoring on colors rather than absolute activity numbers. The mechanism takes user input from a *Cluster Control* worksheet, e.g., as shown in **FIGURES 11A-11B**. **FIGURE 11B** shows a control panel from the cluster control worksheet shown in **FIGURE 11A**, wherein the user has selected columns F to I of worksheet "DEMO 1" for scoring dose-response.

The system detects uncolored data, notifies the user, and asks whether to continue. If yes, the system skips the row containing the uncolored data. The system inserts three new columns on the original spreadsheet to contain the new scores, the new columns immediately following the columns of dose-response data. The column headings show the name of the parameter set used for scoring. Preferably, the system offers to regenerate existing table of Sheet Statistics to correct it for newly added score columns. Further, the system offers to sort the data rows by decreasing score. The system also offers to carry out quantitative estimates of IC_{50} values for the user's compounds, by adding artificial calculated calibration marker compounds.

In order to score and sort dose-response data:

(1) Ensure that the dose-dependent activity data columns are ordered with highest concentration at the left and lowest concentration at the right. To ensure this, the system will remind the user of this requirement and ask him to confirm it when this tool is run. *Note*: If the data are for an undesired effect such as toxicity, the columns should be ordered the opposite way (lowest concentration left, highest right).

(2) Use the Data Coloring (described above) to color the dose-response data columns.

(3) Go to the Cluster Control sheet **314** (**FIGURES 11A-11D**) and pick a control panel **1100** to use. On this sheet, a single control panel extends vertically through the black, blue, red, and green sections, and provides input information for several tools.

(4) In the top black section, give this new parameter set a name (**1102**) if not already done. The name will be used to label the outputs.

(5) In the blue section, enter a sheet name (**1104**).

(6) In the red section (**1110**), enter the colors used to color the dose-dependent data, and relative point scores (**1112**) to be assigned to these colors.

(7) In the green section (**1118**), enter the columns which contain the dose-response data (using the same syntax as for Data Coloring).

(8) Click the green-text "Score Dose-Response" button (**1120**).

(9) If the data are expressed as "percent of maximal effect," the user can follow the prompts to add calibration markers and make quantitative estimates of IC_{50}'s.

<u>Note</u> on the output of score and sort dose-response: the system inserts three score columns after the dose-dependent data. The three scores are all scaled to a 0-100 range, and have meanings as follows:

(a) degree of dose-responsiveness over the concentration range tested:

100 = smoothly decreasing with dilution, spanning the entire range of color groups;

75 = flat dose-response; and

<75 = even more poorly behaved

(b) overall activity level demonstrated in the dose-response data

100 = highest activity color group at all concentrations.

(c) a variably weighted composite of (a) and (b), designed to give high scores for high activity even when dose-responsiveness is poor (e.g. a compound that is highly active at all concentrations).

The Dose-Responsiveness Scoring Algorithm

The data columns are ordered left to right, by decreasing concentration. The scoring algorithm awards positive score points for each dilution step across the data that actually shows a decrease in the activity data *group* (i.e., the color), and to penalize every step that does not. The algorithm uses the following scoring:

- +1 point (awarded) when a dilution step moves to a lower activity group
- 0 points when a dilution step leaves the activity group unchanged
- -3 points (penalty) when a dilution step moves to a higher activity group

The maximum score would go to a compound that shows all the possible color group steps in the right direction, and has no reversals. The minimum score would go to a compound with all the possible reversals, and no correct steps. The program then scales the extremes to 100 and 0, in order to present a consistent interface to the user.

The relative magnitudes of the scoring parameters were empirically arrived at by testing "complete sets" of color patterns. This is possible because of the data simplification afforded by the value grouping. If we define the following numerical parameters:

$C \equiv$ number of colors used, i.e., number of data value groups

P ≡ number of points measured, i.e., number of different concentrations (doses) tested,

then the entire "universe" of possible color patterns includes (C^P) different cases. For some typical values that might be encountered in real HTS data, this total number of cases is manageable in **EXCEL**, as shown by **TABLE 1**, below.

TABLE 1. Total Number of Color Patterns

P = # of conc. Points	C = # of color groups	total number of possible cases
3	3	27
3	4	64
4	3	81
4	4	256
5	3	243
5	4	1024
6	3	729
6	4	4096
7	3	2187
7	4	16384*

* For a spreadsheet with a heading row, this exceeds **EXCEL**'s current limit (for EXCEL 95) by one. This value should not exceed the limit for Excel 97.

Scoring was done on several of these complete sets. In each set, the results were sorted by decreasing score and compared to "intuition" for general correctness of ordering of dose-responsiveness, and scanned for cases deemed to be clearly out of order. The (+1, -3) score set was found to produce satisfying ordering, while lesser penalties led to poorly ordered results. More objective tests of ordering (described below) were then used to further validate the algorithm

The case of P=3 and C=3 is presented below in its entirety for illustration. **TABLE 2** (**FIGURE 16F**) shows artificial data and processing for twenty seven (27) hypothetical compounds. The "percent inhibition" columns represent assay "data." If one defines three groups by breakpoints at 33% and 66%, each cell is

assigned to a data group as shown in the middle set of three columns. Here it is clear that the order of compounds in this table is systematic (111, 112, etc.), to illustrate that the complete set is present. The third set of three columns shows color coding, with the darkest being least active and the lightest being most active.

Then the data set was processed by the system to yield dose-responsiveness scores, and the results sorted by this score, giving **TABLE 3** (**FIGURE 16G**), the complete set in order of decreasing dose-responsiveness. **TABLE 3** also shows the intermediate step-scoring and unscaled score points, to aid in following and understanding the algorithm. These points are not displayed by the system itself.

The Overall-Activity Scoring Algorithm

The second property of interest to be extracted from the data is the overall activity level exhibited by each compound. As explained above, this is largely independent of the dose-responsiveness.

The data value groups' ordinal index numbers are used as single-point activity measures instead of the original data numbers. Extra weight is given to activity shown at lower concentrations by the simple algorithm of weighting each data column by its serial position, again ignoring the actual concentration values. The scores are then scaled to the range 0 to 100. The results of this scoring on the same complete set are shown in **TABLE 4** (**FIGURE 16H**) which has been re-sorted by decreasing overall activity.

The Composite Scoring Algorithm

Comparison of Tables 3 and 4 (**FIGURES 16G & 16H**) shows clearly that the compound ordering by dose-responsiveness is quite different from the ordering by overall activity. The user (a chemist) could now color-code the new score columns and use them as independent factors in a larger scoring. However, chemists also want a *single* index of compound quality derived from the dose-dependent data. Moreover, a composite index would further help to alleviate the effects of noise on data interpretation, by incorporating more information into the ordering process. This is an "information-based smoothing" of the data. Therefore, a procedure to calculate a third, "smart composite" score from the other two scores was devised.

The general idea is that when selecting good compounds from dose-response data, compounds showing overall high activity should not be discarded for lack of responsiveness. Therefore, the smart composite score should give more weight to the overall activity when the overall activity is high, but lower weight when it is low. A generalized weighted average is written as

$$\textit{composite score} = \textit{(activity weight)(activity score)} + \textit{(responsiveness weight)(responsiveness score)}$$

or, defining corresponding symbols:

$$S_C = (W_A)(S_A) + (W_R)(S_R)$$

If the weights are normalized to sum to unity, then this becomes

$$S_C = (W_A)(S_A) + (1 - W_A)(S_R)$$

The activity weight W_A varies with the activity score S_A in such a way as to achieve the desired result.

The functional form of this variation was the subject of empirical testing. It was decided that the limits would be that W_A would approach 0.5 (activity and responsiveness equally weighted) in the limit of low activity, and that W_A would approach 1.0 (responsiveness ignored) in the limit of high activity. The actual variation was encoded as an exponential increase in order to have rather sharp onset of the activity bias at higher activities:

$$W_A = (C_1) \exp [(k)(S_A)] + C_2$$

The value of the coefficient $k=0.06$, for which the activity bias starts to become substantial around an activity score of eighty (80), was chosen for implementation in a preferred embodiment of this invention, according to empirical results. **FIGURE 16I** shows the variation for a few values of k. **TABLE 5** (**FIGURE 16J**) shows all three scores for the example complete set, now sorted by decreasing composite score.

The details of the scoring algorithms were arrived at largely by comparing results to intuitive ordering of the test cases in the complete sets. Because the sets were complete, no really new results can be generated by further test sets. However, one can generate test activity data sets from compounds of known potencies, whose real rank ordering is thus known, in order to see more objectively how well the scoring algorithms rank the results.

To this end, a set of pseudo-ligands was hypothesized, with dissociation constants from a fictitious receptor ranging from nanomolar to millimolar (pK = 9 to 3). The set included thirty one (31) compounds, with potencies evenly spaced by 0.2 log units (9.0, 8.8, 8.6, ... , 3.4, 3.2, 3.0). A "pseudo-screen" was created which "tested" binding of these ligands at five concentration points in the usual

range: 10^{-5} M, $3x10^{-6}$ M, 10^{-6} M, $3x10^{-7}$ M, and 10^{-7} M. Note that the span of potencies exceeds the span of concentrations tested by two log units on each end, so the test set includes both "very active" and "very inactive" compounds relative to the screening concentrations.

Then artificial binding data were created by calculation as follows. Assuming a simple binding equilibrium of the ligand to a receptor, the "percent inhibition" at a given ligand concentration is equal to the fraction of receptor sites which are occupied by ligand, given by simple equilibrium equations as

$$p_{inhib} = 100 \bullet (\text{ligand}) / [K + (\text{ligand})]$$

For a more realistic simulation, artificial random noise was then added to the calculated numbers. The first experiment reported below used noise randomly distributed over the range of ±10 inhibition percentage points, and the second with noise up to ±30 inhibition percentage points. Note that this means ten or thirty percentage points of absolute error, not 10% or 30% of the value.

The artificial data were then color-coded according to the mechanisms of this invention (described above) into four color groups, using the simple breakpoints at 25, 50 and 75 percent inhibition. Note that in assigning these breakpoints, no consideration was given to the actual data values. Then the scoring algorithms of this invention were run, and the compounds sorted by the composite score. Rank order numbers were assigned to the compounds, with 1 being the most potent and 31 the least. In cases of ties in the composite score, equal rank numbers were assigned, with a value equal to the average of the rank numbers spanned by the tied group of compounds (e.g., a tie for 2nd and 3rd

would result in each compound being ranked "2.5"). For each experiment, the final rankings were plotted against the "real" rankings by known potency, to test how well the scoring algorithms ordered the compounds. These plots are shown in **FIGURE 16K** (for noise=10) and **FIGURE 16L** (for noise=30).

For the experiment with noise up to 10 inhibition percentage points, shown in **FIGURE 16K**, the ranking of the composite scores is "perfect" (in the sense of having no inversions) over the range of tested concentrations (pK = 5 to 7). The pseudo-screen is unable to distinguish the potencies of compounds above or below this range.

When the noise is much higher (30 percentage points), the ranking of individual compounds is not as precise, but one can identify three cleanly divided "good-medium-bad" groups, as indicated by the dashed boxes on **FIGURE 16L.** Thus, even with this rather extreme noise level, the invention's scoring still successfully prioritizes the compounds into groups. The range where discrimination is effective is still roughly the range of the test concentrations (pK = 5 to 7), but has been reduced somewhat by the higher noise. Note that the ranking within this range (the middle boxed group) is still mostly correct, with only one inversion, even for single compounds.

Quantitative Estimation of Potencies

With confidence established that the algorithms provide reliable rankings of compounds by potency, it is possible to proceed to making quantitative estimates. The method uses calibration marker compounds.

To understand this method, it is helpful to realize that the concept is analogous to the quantitative use of SDS polyacrylamide electrophoresis gels to

measure protein molecular weights. The proteins are known to migrate through the gel with speeds directly dependent on molecular weight, but it is difficult to calculate the absolute migration rates for a particular experiment. In dose-response scoring, the compounds are known to be properly ordered, but it is not clear how to calculate a potency (e.g., K_{diss} or IC_{50}) directly from the score.

Protein chemists solve the molecular weight problem by running marker proteins, with know molecular weights, in the same gel, then using their band positions as calibration for the unknowns. Analogously, this invention's quantitative estimation method uses hypothetical marker compounds of know potency to internally calibrate the dose-response composite scores for the user's choice of a coloring rule, then interpolates the potencies of the unknowns.

To create markers, the system asks the user to input the concentrations used for each of the dose-dependent activity data columns. The system then picks a set of calibration concentrations, at intervals of 0.5 log units, to span the tested range. For each of these calibration concentrations, a marker compound is created and added to the user's compound list, and artificial data is calculated for each column, from the same simple equilibrium binding equation used above in the validation study (this time with no "noise"):

$$p_{inhib} = 100 \bullet (\text{ligand}) / [K + (\text{ligand})]$$

The marker data are then colored by the same rule used for the user's compounds, and the scoring and sorting algorithm is re-run.

The result is that the markers are sorted into the list according to their potencies, and the potencies of the other compounds can be estimated by

interpolating between the markers, using the composite dose-response scores. To illustrate, a typical section of a sorted list is shown below in **Table 6** (**Figure 16M**), using four colors.

Potencies for compounds that fall between two markers are calculated by linear interpolation between the logarithms of the markers. Given the various uncertainties in the data values themselves and in the evaluation process, it was found that linear interpolation between markers spaced at 0.5 log unit intervals was sufficiently precise, and no more complex curve fitting was necessary.

Validation of Quantitative Estimation

Validation of the quantitative estimation method followed a procedure very similar to that used to validate the scoring, and using the same sets of test data with various noise levels. As before, the testing concentrations were from 10^{-5} to 10^{-7} M (negative log from 5 to 7). Marker compounds (no noise) were added with pK's from 4.5 to 7.5, and K_{diss} estimates for the noisy compounds were carried out by the interpolation method. The results are shown below for the cases of 10 and 30 inhibition percentage points of noise.

Figures 16N and **16P** show that the estimates are clearly quite good within the range of the testing concentrations (pK 5 to 7), but the quality of estimation deteriorates quickly beyond those limits, and algorithm does not reliably distinguish among compounds whose potencies are more than a half log unit beyond the testing range. Therefore, it was decided that presently preferred embodiments would not report any estimated values that fell outside the range of concentrations used in the testing data columns. Thus, in the example in **Table 6** (**Figure 16M**), the lowest testing concentration was 10^{-7} M (= 0.1 μM). For the

first compound in **TABLE 6**, the system has estimated a potency with $pIC_{50} > 7$, but it conservatively only reports "<0.1 μM."

TABLE 7 summarizes the statistics of the estimations within the testing limits. **TABLE 7** shows that the method successfully estimates the potencies within about a factor of two, even with high noise levels.

TABLE 7. STATISTICS OF ESTIMATION VALIDATIONS

percentage points of noise	*number of compounds*	*average of abs(log error)*	*Average error in IC_{50} (factor)*
10	13	0.22	x 1.6
30	13	0.39	x 2.5

Comparison to Other Methods of Quantitative Estimation

Further corroboration was obtained by treating some real data from T-cell proliferation blockage assays. It is estimated that these data have *at least* as much noise as the artificial test set with 30 inhibition percentage points added. The standard treatment of this data in the past has been to fit a dose-response curve with a Hill coefficient of 1, using a PC-based program ORIGIN. (ORIGIN is a data analysis program from Microcal Software, Inc. of Northampton, Massachusetts. ORIGIN is used in this instance for non-linear least-squares fitting of dose-response curves to functional equations.)

The data used here were from testing in the concentration range from 1 to 0.03 μM (negative log from 6 to 7.5). The plot in **FIGURE 16Q** shows the correlation of values estimated by this invention with values from ORIGIN fits.

Two compounds that the present invention estimates to be beyond the testing range, i.e., pIC_{50} below 6, are included as open diamonds, for illustrative purposes explained below. (As explained above, preferred embodiments of this invention would normally not report these values.)

The results are consistent with the properties observed in the validation study. The present invention estimates are quite good within the testing range (6 to 7.5). At the lower limit, this invention has made two estimations exactly at 10^{-6} M (arrows) which do not correlate as well with the ORIGIN fits. Nevertheless, because the whole plot spans only a relatively narrow range of potency, even these discrepancies are not very large. For all twenty eight (28) estimates within the testing range (including these two), the average logarithmic deviation between the two estimation methods is 0.18, corresponding to a factor of only 1.5.

It is further noted that the calibration marker estimation method does not uniformly "flatten out" beyond the testing concentration range. The two open diamonds in **FIGURE 16Q** are estimations that presently preferred embodiments of this invention would not normally report because they have $pIC_{50} < 6$, but they agree well with ORIGIN fits

It is interesting to compare calibration-marker with curve-fitting results for particularly badly behaved data, such as dose-response curves that are not monotonic with respect to concentration. This is sometimes the type of data that emerges from dose-dependent screening in a high-throughput mode. Studies of this type have been initiated by adding artificial noise to the extent of fifty (50) inhibition percentage points.

Finally, it should be pointed out that there is some mechanical advantage to using the present invention relative to current practice of using ORIGIN.

ORIGIN is used by manually filling in a template with data, then manually executing a fit. Depending on the number of points and the degree of customization of parameters, this can take one to ten minutes of the user's time. The present invention, on the other hand, processes a whole spreadsheet at once (i.e., up to 16,383 compounds), and goes at a rate of about 3,000-4,000 compounds per minute on a 200 MHz PC.

Examples

FIGURE 16A shows dose response data for twenty (20) compounds at four concentrations. The data have been grouped and the cells colored by the rule shown in **FIGURE 16B**. The result of the scoring and sorting process is shown in **FIGURE 16C**, where the compounds are ordered by decreasing values of the composite score (column H). Then, virtual "marker" compounds are added with known potencies spaced by 0.5 log units, and they are shown in **FIGURE 16D**, colored by the same rule and scored. The name of each marker compound designates the logarithm of its potency, e.g., "marker_7.0" has a potency $IC_{50} = 10^{-7}$ M. **FIGURE 16E** shows the result of sorting the list by decreasing composite score after adding the markers. This process then enables estimation of IC_{50} values for the compounds by interpolating in the column (H) of ordered composite scores, and these estimates appear in two forms in columns I and J.

6. Summarize Spreadsheet Statistics Mechanism

This mechanism creates a table summarizing the entries in each column of a data sheet, to aid the user in deciding how to color each column. The

mechanism counts numeric, text, and data entries, and uses color to flag columns that have mixed types. The mechanism also counts blanks, and specially flags columns with "trailing blanks," i.e., columns which are shorter than the longest one on the spreadsheet. For numeric data, the mechanism calculates minimum, maximum, mean, and standard deviation, even in the presence of interspersed text entries. For text data, the mechanism presents a list of the text strings used and their occurrence counts. The mechanism creates a summary key of the column letters and headings as a text box that can be copied to other sheets for convenient reference.

FIGURE 17A shows a sample spreadsheet containing miscellaneous data on twenty four (24) compounds. **FIGURE 17B** is the statistics sheet calculated from it. Each row of the statistics sheet describes one column of the original data sheet. First, the counts of numeric, text, date, and blank entries are listed, followed by two columns describing the total length of the data sheet. Then the minimum, maximum, mean, and standard deviation of any numeric data are reported. Finally, the statistics sheet lists a summary of the text strings found in each original data column. As examples, in **FIGURE 17B**, one can see that original column A ("Cmpd") had twenty four (24) different text strings, that the numeric data in original column C ("Test1") had a mean of 2.385, and, flagged by the red coloring, that original data column E ("Test3") had a mixture of ten numeric data and two text strings, both "N.A."

The details of how the program code accomplishes this are straightforward, and one of ordinary skill in the art would know, from this description, including the Figures, how to make and use this invention. The

program loops through all the entries in the column, testing the data type of each, and tallying the counts and numerical statistics.

Spreadsheet Creation and Organization

The operations of this invention require a considerable amount of user input, e.g., to create well-structured spreadsheets, to define and apply diverse coloring rules for large numbers of columns, and to use these colors and the user's stated scientific priorities to create meaningfully ordered lists of compounds or clusters.

The user interface of this invention has been designed to ease this process and help the scientist focus on the tasks of formulating and recording clear descriptions of the evaluation parameters. Accordingly, this invention provides a number of tools and mechanisms to aid in the creation and organization of spreadsheets. These tools and mechanisms include:

- Smart Append Column Mechanism
- Merge Data Mechanism
- Data Import Mechanism
- Workbook Navigation Shortcuts
- Conversion of "uM" to µM and "UU" to µ
- Delete Pictures Mechanism
- Change Values in Column Mechanism
- Concatenate Values across Columns Mechanism
- Delete Leading Inequality Signs Mechanism
- Delete Derived Sheets Mechanism

Smart Append Column

This mechanism appends new columns of data onto an existing spreadsheet, matching rows by labels (e.g., compound numbers). The mechanism copies all data to a new sheet before doing its work, leaving the original sheets unchanged. There is no need for the user to pre-sort any of the data. The mechanism provides optional case-sensitive or case-insensitive label matching.

New rows are added at the bottom when new labels do not match any old labels. Rows with missing labels are identified and the system offers to fill them by copying previous label. Rows with repeated labels (i.e., replicate data) are also identified and the system offers a choice from among several automated processing rules, or manual fixing. A fast matching algorithm temporarily sorts rows by label, then restores original order when finished. Several intermediate stopping points are offered and extra data viewing options for conservative users worried about errors.

Merge Data Mechanism

The merge data mechanism copies new data values from an appended column into an older column. The mechanism copies all data to a new sheet before doing its work, leaving the original sheets unchanged. The mechanism detects cells where new data would overwrite old data that is different, flags them with color, and alerts the user. Several intermediate stopping points are offered to

the user, as are extra data viewing options are offered for conservative users worried about errors.

Data Import

One-button (or one-menu-click) import of existing EXCEL spreadsheets into an integrated file, which contains both the data and the related control sheets. The mechanism offers to search for and remove any leading or trailing spaces in the imported data and offers to consolidate replicate data rows into unique ones, using user choices as to how to handle the replicate data. The mechanism also detects hidden rows and offers to unhide them and detects formulas and offers to convert them to values. This mechanism is also used to update to newer version of the system.

Workbook Navigation Shortcuts

The system includes various workbook navigation shortcuts including:

- A special added drop-down menu which includes commands for jumping directly to the various control sheets. These commands also have keyboard shortcuts assigned to them.
- From a cell on a control sheet that contains the name of a data sheet, a special item on the right-click shortcut menu jumps directly to that data sheet. Other special items on this menu enable a "Twin Screen" display to see two sheets at once.

- To aid in choosing columns to enter on control sheets, there is a special "Twin Screen" display triggered by right-clicking any cell on a control sheet that contains the name of a data sheet.

Convert "uM" to µM and "UU" to µ

Preferred embodiments of the system of this invention require the data spreadsheet to have *one and only one* row of column headings. The user can type either of the encoded strings "uM" (lowercase u, uppercase M) or "UU" (both uppercase) into any column heading, select the cell or whole row of headings, then pick this command. Each "uM" in the selection will be converted to "µM", and each "UU" will be converted to a "µ". The code recognizes the special exception of the word "VACUUM" as long as it doesn't end with the cases "uM." This conversion allows the user to avoid the confusing use of lowercase "u" or the column-widening use of the full prefix "micro." This utility appears on the system menu.

Delete Pictures

The system provides a mechanism for removing pictures containing chemical structures, in order to reduce file size, processing time, and confusion when they do not align properly after row sorting.

Change Values in Column

This is a mechanism for regularizing data in a spreadsheet column. It facilitates replacement of all occurrences of a given value by another. The mechanism creates backup copies of the original column, and updates any existing data statistics for the edited sheet.

Concatenate Values across Columns

The system provides a mechanism for regularizing data in a spreadsheet column. Some possible uses include: (a) construction of unique row labels: M-number plus stroke number → "M123456/001"; and (b) reconstitution of numerical inequalities from separate columns: ">" plus a number → ">number". The user is provided with an option to include linking (delimiting) text strings between values and an option to include or skip blanks. The system retains the original columns and inserts a new one for the results.

Delete Leading Inequality Signs

Another mechanism for regularizing data in a spreadsheet column includes the mechanism to delete leading inequality signs. This mechanism converts entries like ">1000" to just the number "1000". This must be used with considerable caution, because it is the equivalent of creating a false test result. It is generally preferable to color the cells containing text strings with the data coloring mechanism described above, rather than alter them. All later processing is based on the colors, not the cell values. This mechanism also deletes inequality

sign only if it is the first character in the cell. The mechanism creates backup copies of the original columns.

Delete Derived Sheets

The system menu includes a command to delete all output sheets from the current workbook, with separate user confirmation for each one. This is intended as a cleanup mechanism for information that may be outdated and is easily regenerated by subsequent system runs.

Initial experience with the coloring tool has revealed that color coding has more subtle, but far-reaching usefulness. The colors themselves also can act as a "currency of exchange," a medium for comparing the quality of one kind of result to the quality of a very different kind of result. For example, an HTS activity of "95% inhibition" may be considered desirable and color coded, e.g., green. In the same list of compounds, a molecular weight between 400 and 600 may be considered optimally desirable, and thus also color-coded green. If the user takes care when assigning colors, "green" takes on a common meaning across the board. This translation of data values into colors then opens up a cornucopia of possibilities for processing the colors (as numerical color indices) and comparing compounds, searching, in our example, for the ones that are the "most green."

Accordingly, the system includes tools to numerically score individual compounds or clusters of compounds by the colors that appear in their various data columns. The system can then create a new spreadsheet sorted by this score

(either by single compounds, or cluster-by-cluster, the choice being the user's), in which the "most green" compounds will then appear at the top.

Examples

Application to Portfolio Management

The system can equally well be applied to any set of data where the rows are cases of a similar construct, with the columns being various properties of each case. For example, a data spreadsheet can contain a list of competing projects or investments for a company's portfolio, with the columns containing various managers' ratings of each project or investment. **FIGURE 18A** shows an example of twenty projects, each of which has been scored 1, 2, or 3 on two factors, one more important than the other, by each of three managers. The sheet has been colored by the rule shown in **FIGURE 18B**. Then the data were scored and sorted by the sorting rule of **FIGURE 18C**, and the result is shown in **FIGURE 18D**. Clearly, the projects that were given a "3" in the important factor come to the top, and it can be seen that the less important factor does indeed matter less to the final ordering. The colors also help to flag anomalies, such as a low score by one manager on an otherwise high-ranking project.

In general, the data can be various sorts of data. Some examples are listed below and illustrated in the referenced Figures.

FIGURE 19 shows a list of drug candidate compounds, scored and sorted by a composite of ten parameters that describe their physical, chemical, and biological properties. Green shades indicated desirable values; red shades are

undesirable. The display is compressed vertically with the vertical re-scaling tool to clearly display the difference in coloring patterns between the top eighty (80) compounds and the bottom eighty (80) compounds (separated in the illustration by a blank band).

FIGURE 20 shows a list of proteins that are candidates for targets for drugs, chosen from a pool of candidate genes, scored and sorted by a composite of eleven parameters that describe their suitability.

FIGURE 21 shows a list of research projects competing for resources. Each project has been scored according to several evaluation factors, and the whole array has been sorted by color groups. The same construct is useful for evaluating employee performance or job candidates.

FIGURE 22 shows a list of pharmaceutical companies and their current status with regard to discovering or marketing products in each of various disease areas. Each company's line of products has been scored according to the maturity of the offerings, and the whole array has been sorted by color groups.

FIGURE 23 shows the use of data-grouping (coloring) rules to visualize the time courses of drug concentrations in blood. In this example, light colors were chosen to represent high concentrations of drug in the blood, while dark colors were chosen to represent low concentrations. The figure shows a wide range of differing time courses.

FIGURE 24 shows the use of data-grouping (coloring) rules to visualize the matrix of pairwise cross-correlations of the results of eight (80) drug screens. In this example, light colors were chosen to represent low correlations, while dark colors represent high correlations.

Quantitation of the Similarity of Data Grouping in Two Variables

As part of the present invention, a mechanism is provided for assigning a quantitative measure to the degree of similarity of grouping (visualized by color coding) of data in each of two columns of an EXCEL spreadsheet. The mechanism allows for a correlation-like analysis on a wide variety of data types, including text, or mixed numbers and text.

In the data-exploration paradigm of the present invention, one of the first steps a user takes is to divide the range of data values in each column into a small number of groups for further analysis, thus effecting a reduction of precision which has been found to be useful in various ways.

It is sometimes useful to explore whether the rows of the data matrix have been divided into similar groupings in each of two different columns. For example, a researcher might ask, "Do the high molecular weight compounds tend to be the ones whose solubilities fall below the limits of measurement?" In other words, this would mean to compare the groupings in the molecular weight column with the groupings in the solubility column.

If the data were strictly quantitative, this would be called *correlation* of variables, and there exist a number of perfectly good statistical measures of the phenomenon. However, one of the unique capabilities of the present invention lies in dealing with textual data and mixtures of numbers and text, and it would be helpful if one could translate the visible color patterns of the present invention to some kind of quantitative measure of correlation. In order to avoid confusion with standard statistical correlation, the distinct term "color grouping similarity" is used to describe the new measure.

In preferred embodiments of this invention, the data grouping is stored in the form of the colored backgrounds of data cells. At first glance, one might simply seek to compare the colors of the first column with those of the second, and count the number of rows with matching colors. However, a color grouping similarity tool must be able to cope with the possibility that the colors are different. This could happen because the user chooses completely *different color schemes* for the two columns, or because the correlation is negative. As an example of negative correlation, suppose column A contains random numbers between 0 and 1, colored such that those above 0.5 are green and those below 0.5 are red. Then imagine a column B where each value is equal to one minus the corresponding value in column A, i.e., the "one's complement." If the user colors the second column with exactly the same coloring rule as the first, every row will have a different color in column B than in column A. None of the colors will match, though the groupings are perfectly correlated. To be successful, the tool must deliver a high measure of correlation between such pairs of columns. The algorithm described below was designed to perform in this way.

Algorithm for Measuring Data Grouping Similarity

The algorithm was derived from semi-quantitative reasoning, as follows. It is based on the qualitative question, "For all rows that have one particular color in the first column, to what degree do they have a *uniform* color in the second column (not necessarily the *same* color as in the first column)?" The quantified answer to this question is then averaged over the set of colors used.

The details of the mechanism can be seen by example. First, to compare the grouping in two columns A and B, a matrix of "ordered color pair counts" (OCPC) is defined such that each matrix element $OCPC_{ij}$ is the count of spreadsheet rows where one finds color i in spreadsheet column A and color j in spreadsheet column B. Then, the rows of the two spreadsheet columns are scanned to count the number of occurrences of each ordered color pair and thus to determine the values of the matrix elements.

In the discussion below, carefully distinguish the rows and columns of the user's *spreadsheet* of data from the rows and columns of the derived OCPC *matrix.*

If the two spreadsheet columns had *exactly the same coloring*, the nonzero elements of the OCPC matrix would all be on the diagonal. As a simplified example, consider four colors (green, yellow, orange, red) and a total of 16 data rows. The diagonal matrix might be (zero elements left blank for emphasis)

color in column A	color in column B →	green	yellow	orange	red
green		4			
yellow			2		
orange				7	
red					3

In the case above, there are groups of 4 spreadsheet rows colored green (in both columns), 2 rows colored yellow, 7 rows colored orange, and 3 rows colored red.

In contrast, if the groupings were the same, but the coloring rule for the second spreadsheet column used the same colors in a different order, the OCPC matrix might look like the following, no longer diagonal:

color in column A	color in column B →	green	yellow	orange	red
green				4	
yellow		2			
orange					7
red			3		

A simple extension applies if *entirely different colors* (cyan, blue, maroon, purple) are used in the second spreadsheet column. The OCPC matrix might then be:

color in column A	color in column B →	cyan	blue	maroon	purple
green				4	
yellow		2			
orange					7
red			3		

In *any* of the three cases above, the groupings are identical, and the OCPC matrices have the property that each matrix row and matrix column has only one nonzero element. That lone element is necessarily equal to the sum of the row or column. This situation should receive the *highest* similarity score.

One way to define the contrasting situation that would deserves the *lowest* similarity score would be that for each user-defined group of spreadsheet rows in one spreadsheet column, the other spreadsheet column has a "maximally non-unique" set of colors. In the corresponding OCPC matrix, this corresponds to each matrix row or column having a broad distribution of values rather than a single non-zero, a uniform distribution has been chosen as the definition of this state:

color in column A	color in column B →	cyan	blue	maroon	purple
green		1	1	1	1
yellow		1	1	1	1
orange		1	1	1	1
red		1	1	1	1

This low-similarity state can be more precisely defined by saying that each element in a given matrix row or column is the average of all the counts in that matrix row or column.

With these concepts defined and the OCPC matrix filled, the scores can then be derived. Each OCPC matrix row (corresponding to a color group in the first spreadsheet column) is selected in turn for scoring. Each element in the matrix row is given a score between zero and one, according to its linear interpolation between: on the one extreme, the average of the nonzero elements in the row, and on the other, the sum of the row or column (i.e., the maximum value it could have if all the others were zero). The scores are then averaged over all the rows of the OCPC matrix to generate a row-wise score component.

Next, the corresponding process is applied to the *columns* of the OCPC matrix (each corresponding to a color group in the second spreadsheet column rather than the first). The resulting column-wise score component is averaged with the row-wise score component, then the average is scaled to a maximum of 100 to generate the final similarity score for the two spreadsheet columns.

Interpretation of the Similarity Scores

Although the scores are quantitative and well-defined, their interpretation is best done in a partly subjective manner, based on experience. The behavior of

the scores is best understood by example. In **FIGURE 25**, the leftmost ("base") column has been compared to each of the others, and the scores are shown as well as pictures of the grouping patterns. Comparison of the base with the next column shows that the tool delivers a maximal score of 100 for identical grouping, even when the colors are completely different. Then, stepping across the figure toward the right, it can be seen how the score decreases as the grouping pattern gradually becomes less similar to that of the base column. All the way down to a similarity score of 40, it is still basically true that the light colors are on top and the dark on the bottom, with increasing "noise," but when the score falls to 20, the pattern appears to have no correspondence to that of the base.

Implementation of the Data Grouping Similarity Tool

In practice, the tool allows the user to choose two sets of spreadsheet data columns. The program then automatically generates all pairs containing a column from the first set with a column from the second set, then writes the similarity scores onto a newly inserted spreadsheet in the user's workbook. The output takes the form of a table where the degree of similarity is itself color-coded to aid the user in identifying significant cases. An example appears **FIGURE 26**.

While the invention has been described with reference to particular mechanisms (algorithms, processes and functions) and architectures, one skilled in

the art would realize that other mechanisms and/or architectures could be used while still achieving the invention.

While embodiments of the present invention have been described with particular setup and initialization procedures, other setup and/or initialization procedures can be used.

Further, while many of the operations have been shown as being performed in a particular order, one skilled in the art would realize that other orders, including some parallelization of operations, are possible and are considered to be within the scope of the invention.

While the present invention has been described with reference to analysis and pattern recognition in data sets relating to chemical compounds, the methods, systems and devices of this invention are considered to be general constructs covering other, non-chemical data sets.

Thus, are provided methods, systems and devices for analysis and pattern recognition in large, multidimensional data sets using low-resolution data grouping. One skilled in the art will appreciate that the present invention can be practiced by other than the described embodiments, which are presented for purposes of illustration and not limitation, and the present invention is limited only by the claims that follow.

What is claimed is:

1. A method of operating on data, the method comprising:

providing at least one user-defined grouping rule for grouping the data into a user-definable number of groups; and

applying at least one of the grouping rules to the data.

2. A method as in claim 1 wherein the data are provided in a table and wherein the at least one grouping rule applies to at least one user-selectable column of the table.

3. A method as in claim 1 wherein the at least one grouping rule defines breakpoints corresponding to the user-definable number of groups, and wherein application of the at least one rule to the data divides the data into groups based on the breakpoints.

4. A method as in claim 1 further comprising:

presenting the grouped data in a manner that visually distinguishes the groups.

5. A method as in claim 4 wherein the grouping rules associate colors with groups and wherein the presenting of the grouped data further comprises:

coloring an aspect of the data according to the rules.

6. A method as in claim 4, wherein the data are in labeled columns in a spreadsheet, and wherein the at least one grouping rule specifies at least one breakpoint and a corresponding color for each at least one breakpoint, and wherein the presenting of the grouped data comprises:

coloring each data item in the at least one labeled column of the data based on the at least one breakpoint and the corresponding color of the at least one breakpoint.

7. A method as in any one of claims 3 and 6, wherein the breakpoints are selected from: (a) numeric values; and (b) textual values.

8. A method as in claim 3 wherein the at least one breakpoint is determined automatically based on the data.

9. A method as in claim 5 wherein the data are provided in a table, wherein the coloring of an aspect of the data comprises:

coloring backgrounds of table cells according to the rules.

10. A method as in claim 1 wherein the number of groups is fewer than a number of possible data values.

11. A method of operating on data, the method comprising:

providing at least one user-defined grouping rule for grouping the data into a user-definable number of groups;

applying at least one of the grouping rules to the data to generate grouped data;

providing at least one user-defined scoring rule for scoring the grouped data according to user-defined scores; and

applying at least one of the scoring rules to the grouped data to score the grouped data.

12. A method of operating on data, the method comprising:

generating grouped data by applying to the data at least one user-defined grouping rule for grouping the data into a user-definable number of groups; and

scoring the grouped data by applying to the grouped data at least one user-defined scoring rule for scoring the grouped data according to user-defined scores.

13. A method according to claim 11 or 12 wherein the data comprises a number of parameters for each of a number of cases and the scoring rule comprises a scoring function of user-selectable parameters and user-defined weights for the selected parameters to be used in scoring the cases, wherein the scoring of the grouped data comprises:

applying the function to the data to obtain a score for each case.

14. A method according to claim 13, further comprising:

sorting the scored cases by score.

15. A method according to claim 14, wherein the scored cases are sorted individually.

16. A method according to claim 14, wherein the scored cases are sorted by cluster.

17. A system for operating on data, the system comprising:

a mechanism constructed and adapted to provide at least one user-defined grouping rule for grouping the data into a user-definable number of groups; and

a mechanism constructed and adapted to apply at least one of the grouping rules to the data.

18. A system as in claim 17 wherein the data are provided in a table and wherein the at least one grouping rule applies to at least one user-selectable column of the table.

19. A system as in claim 17, wherein the at least one grouping rule defines breakpoints corresponding to the user-definable number of groups, and wherein application of the at least one rule to the data divides the data into groups based on the breakpoints.

20. A system as in claim 17, further comprising:

a mechanism constructed and adapted to present the grouped data in a manner that visually distinguishes the groups.

21. A system as in claim 20, wherein the grouping rules associate colors with groups and wherein the mechanism constructed and adapted to present the grouped data further comprises:

a mechanism constructed and adapted to color an aspect of the data according to the rules.

22. A system as in claim 20, wherein the data are in labeled columns in a spreadsheet, and wherein the at least one grouping rule specifies at least one breakpoint and a corresponding color for each at least one breakpoint, and wherein the mechanism constructed and adapted to present the grouped data comprises:

a mechanism constructed and adapted to color each data item in the at least one labeled column of the data based on the at least one breakpoint and the corresponding color of the at least one breakpoint.

23. A system as in any one of claims 19 and 22, wherein the breakpoints are selected from: (a) numeric values; and (b) textual values.

24. A system as in claim 19 further comprising:

a mechanism constructed and adapted to determine at least one breakpoint automatically, based on the data.

25. A system as in claim 21 wherein the data are provided in a table, wherein the mechanism constructed and adapted to color an aspect of the data comprises:

a mechanism constructed and adapted to color backgrounds of table cells according to the rules.

26. A system as in claim 17 wherein the number of groups is fewer than a number of possible data values.

27. A system of operating on data, the system comprising:

a mechanism constructed and adapted to provide at least one user-defined grouping rule for grouping the data into a user-definable number of groups;

a mechanism constructed and adapted to apply at least one of the grouping rules to the data to generate grouped data;

a mechanism constructed and adapted to provide at least one user-defined scoring rule for scoring the grouped data according to user-defined scores; and

a mechanism constructed and adapted to apply at least one of the scoring rules to the grouped data to score the grouped data.

28. A system of operating on data, the system comprising:

a mechanism constructed and adapted to generate grouped data by applying to the data at least one user-defined grouping rule for grouping the data into a user-definable number of groups; and

a mechanism constructed and adapted to score the grouped data by applying to the grouped data at least one user-defined scoring rule for scoring the grouped data according to user-defined scores.

29. A system according to claim 27 or 28 wherein the data comprises a number of parameters for each of a number of cases and the scoring rule comprises a scoring function of user-selectable parameters and user-defined weights for the selected parameters to be used in scoring the cases, wherein the mechanism constructed and adapted to score of the grouped data comprises:

a mechanism constructed and adapted to apply the function to the data to obtain a score for each case.

30. A system according to claim 29, further comprising:

a mechanism constructed and adapted to sort the scored cases by score.

31. A system according to claim 30, wherein the scored cases are sorted individually.

32. A system according to claim 30, wherein the scored cases are sorted by cluster.

33. A computer-readable memory medium encoded with program data representing a computer program that can cause a computer to implement a method of operating on data, the method comprising:

providing at least one user-defined grouping rule for grouping the data into a user-definable number of groups; and

applying at least one of the grouping rules to the data.

34. A medium as in claim 33 wherein the data are provided in a table and wherein the at least one grouping rule applies to at least one user-selectable column of the table.

35. A medium as in claim 33 wherein the at least one grouping rule defines breakpoints corresponding to the user-definable number of groups, and wherein application of the at least one rule to the data divides the data into groups based on the breakpoints.

36. A medium as in claim 33, wherein the method further comprises:

presenting the grouped data in a manner that visually distinguishes the groups.

37. A medium as in claim 36 wherein the grouping rules associate colors with groups and wherein the presenting of the grouped data further comprises:

coloring an aspect of the data according to the rules.

38. A medium as in claim 36, wherein the data are in labeled columns in a spreadsheet, and wherein the at least one grouping rule specifies at least one breakpoint and a corresponding color for each at least one breakpoint, and wherein the presenting of the grouped data comprises:

coloring each data item in the at least one labeled column of the data based on the at least one breakpoint and the corresponding color of the at least one breakpoint.

39. A medium as in any one of claims 35 and 38, wherein the breakpoints are selected from: (a) numeric values; and (b) textual values.

40. A medium as in claim 35 wherein the at least one breakpoint is determined automatically based on the data.

41. A medium as in claim 37 wherein the data are provided in a table, wherein the coloring of an aspect of the data comprises:

coloring backgrounds of table cells according to the rules.

42. A medium as in claim 33 wherein the number of groups is fewer than a number of possible data values.

43. A computer-readable memory medium encoded with program data representing a computer program that can cause a computer to implement a method of operating on data, the method comprising:

providing at least one user-defined grouping rule for grouping the data into a user-definable number of groups;

applying at least one of the grouping rules to the data to generate grouped data;

providing at least one user-defined scoring rule for scoring the grouped data according to user-defined scores; and

applying at least one of the scoring rules to the grouped data to score the grouped data.

44. A computer-readable memory medium encoded with program data representing a computer program that can cause a computer to implement a method of operating on data, the method comprising:

generating grouped data by applying to the data at least one user-defined grouping rule for grouping the data into a user-definable number of groups; and

scoring the grouped data by applying to the grouped data at least one user-defined scoring rule for scoring the grouped data according to user-defined scores.

45. A medium according to claim 43 or 44, wherein the data comprises a number of parameters for each of a number of cases and the scoring rule comprises a scoring function of user-selectable parameters and user-defined weights for the selected parameters to be used in scoring the cases, wherein the scoring of the grouped data comprises:

applying the function to the data to obtain a score for each case.

46. A medium according to claim 44, the method further comprising: sorting the scored cases by score.

47. A medium according to claim 46, wherein the scored cases are sorted individually.

48. A medium according to claim 46, wherein the scored cases are sorted by cluster.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
1 February 2001 (01.02.2001)

PCT

(10) International Publication Number
WO 01/08039 A2

(51) International Patent Classification[7]: G06F 17/00

(21) International Application Number: PCT/US00/20401

(22) International Filing Date: 27 July 2000 (27.07.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/361,122 27 July 1999 (27.07.1999) US

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

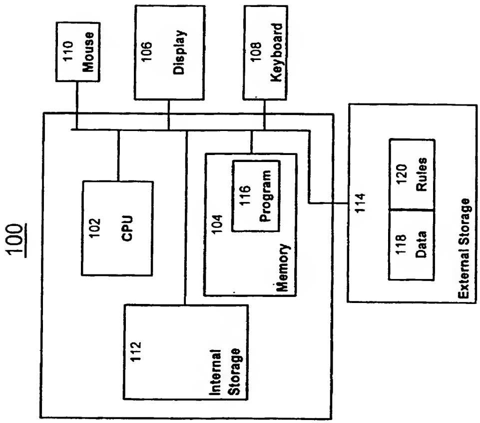
Published:
— *Without international search report and to be republished upon receipt of that report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ANALYSIS AND PATTERN RECOGNITION IN LARGE, MULTIDIMENSIONAL DATA SETS USING LOW-RESOLUTION DATA GROUPING

(57) Abstract: Methods, systems and devices for operating on data provide at least one user-defined grouping rule for grouping the data into a user-definable number of groups; and apply at least one of the grouping rules to the data. The data may be in a table, wherein the at least one grouping rule applies to at least one user-selectable column of the table. The grouping rule defines breakpoints corresponding to the user-definable number of groups, and application of the at least one rule to the data divides the data into groups based on the breakpoints. The grouped data is presented in a manner that visually distinguishes the groups, sometimes by coloring an aspect of the data according to the rules.

WO 01/08039 A2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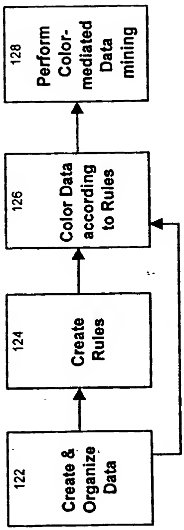
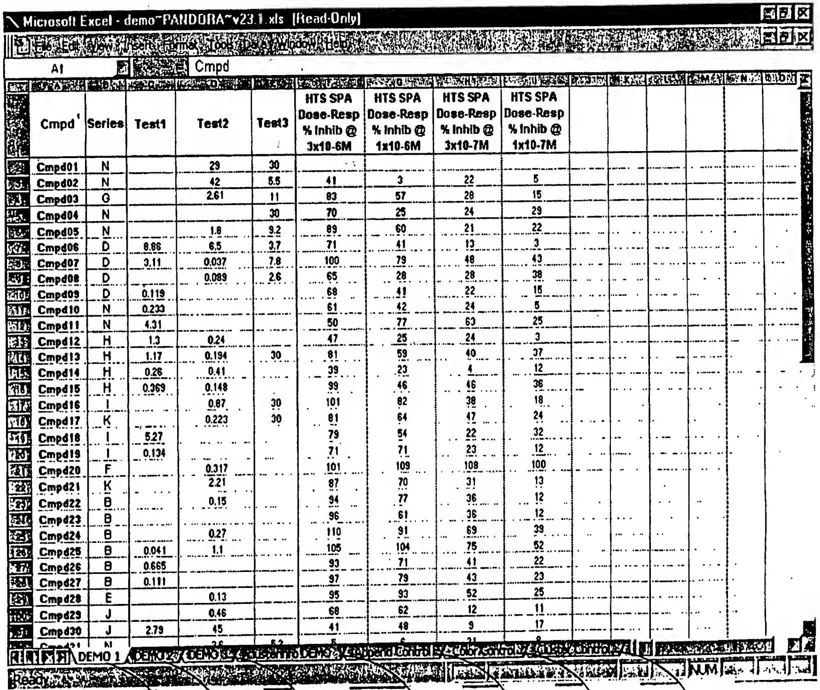
110 Mouse
106 Display
108 Keyboard
102 CPU
104 Memory
116 Program
112 Internal Storage
114
118 Data
120 Rules
External Storage

Fig. 1

Fig. 2


122
Create & Organize Data
124
Create Rules
126
Color Data according to Rules
128
Perform Color-mediated Data mining

300

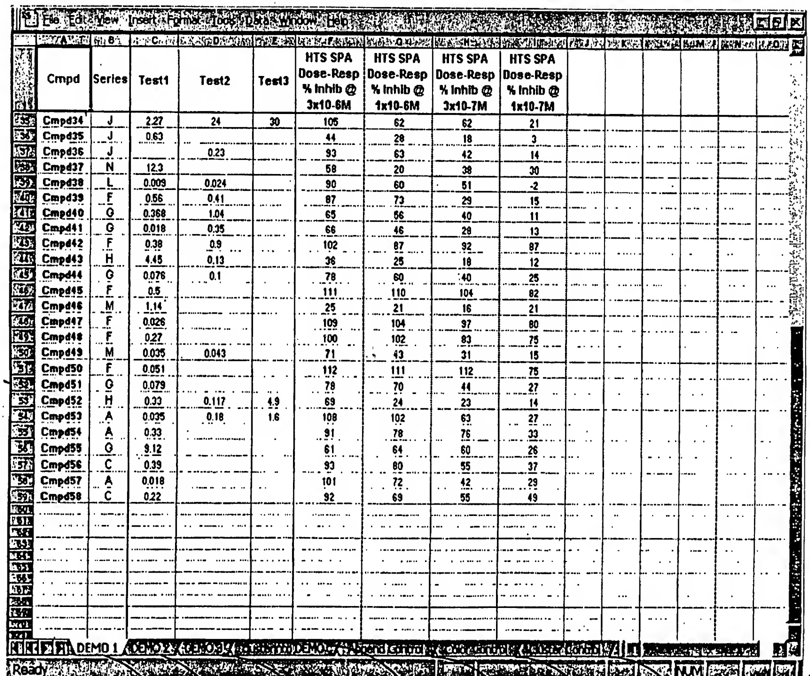


Cmpd	Series	Test1	Test2	Test3	HTS SPA Dose-Resp % Inhib @ 3x10-6M	HTS SPA Dose-Resp % Inhib @ 1x10-6M	HTS SPA Dose-Resp % Inhib @ 3x10-7M	HTS SPA Dose-Resp % Inhib @ 1x10-7M
Cmpd01	N		29	30				
Cmpd02	N		42	5.5	41	3	22	5
Cmpd03	G		2.61	11	83	57	28	15
Cmpd04	N			30	70	25	24	29
Cmpd05	N		1.8	9.2	89	60	21	22
Cmpd06	D	8.86	6.5	3.7	71	41	13	3
Cmpd07	D	3.11	0.037	7.8	100	79	48	43
Cmpd08	D		0.089	2.6	65	28	28	38
Cmpd09	D	0.119			68	41	22	15
Cmpd10	N	0.233			61	42	24	5
Cmpd11	N	4.31			50	77	63	25
Cmpd12	H	1.3	0.24		47	25	24	3
Cmpd13	H	1.17	0.194	30	81	59	40	37
Cmpd14	H	0.26	0.41		39	23	4	12
Cmpd15	H	0.369	0.148		99	46	46	36
Cmpd16	I		0.87	30	101	82	38	18
Cmpd17	K		0.223	30	81	64	47	24
Cmpd18	I	5.27			79	54	22	32
Cmpd19	I	0.134			71	71	23	12
Cmpd20	F		0.317		101	109	108	100
Cmpd21	K		2.21		87	70	31	13
Cmpd22	B		0.15		94	77	36	12
Cmpd23	B				96	61	36	12
Cmpd24	B		0.27		110	91	69	39
Cmpd25	B	0.041	1.1		105	104	75	52
Cmpd26	B	0.665			93	71	41	22
Cmpd27	B	0.111			97	79	43	23
Cmpd28	E		0.13		95	93	52	25
Cmpd29	J		0.46		68	62	12	11
Cmpd30	J	2.79	45		41	48	9	17
Cmpd31	N	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

302 304 306 308 310 312 314

Fig. 3A

300



Cmpd	Series	Test1	Test2	Test3	HTS SPA Dose-Resp % Inhib @ 3x10-6M	HTS SPA Dose-Resp % Inhib @ 1x10-6M	HTS SPA Dose-Resp % Inhib @ 3x10-7M	HTS SPA Dose-Resp % Inhib @ 1x10-7M
Cmpd34	J	2.27	24	30	105	62	62	21
Cmpd35	J	0.63			44	28	18	3
Cmpd36	J		0.23		93	63	42	14
Cmpd37	N	12.3			58	20	38	30
Cmpd38	L	0.009	0.024		90	60	51	-2
Cmpd39	F	0.56	0.41		87	73	29	15
Cmpd40	G	0.368	1.04		65	56	40	11
Cmpd41	G	0.018	0.35		66	46	28	13
Cmpd42	F	0.38	0.9		102	87	92	87
Cmpd43	H	4.45	0.13		36	25	18	12
Cmpd44	G	0.076	0.1		78	60	40	25
Cmpd45	F	0.5			111	110	104	82
Cmpd46	M	1.14			25	21	16	21
Cmpd47	F	0.026			109	104	97	80
Cmpd48	F	0.27			100	102	83	75
Cmpd49	M	0.035	0.043		71	43	31	15
Cmpd50	F	0.051			112	111	112	75
Cmpd51	G	0.079			78	70	44	27
Cmpd52	H	0.33	0.117	4.9	69	24	23	14
Cmpd53	A	0.035	0.18	1.6	108	102	63	27
Cmpd54	A	0.33			91	78	76	33
Cmpd55	G	9.12			61	64	60	26
Cmpd56	C	0.39			93	80	55	37
Cmpd57	A	0.018			101	72	42	29
Cmpd58	C	0.22			92	69	55	49

302 304 306 308 310 312 314

Fig. 3B

10/048022

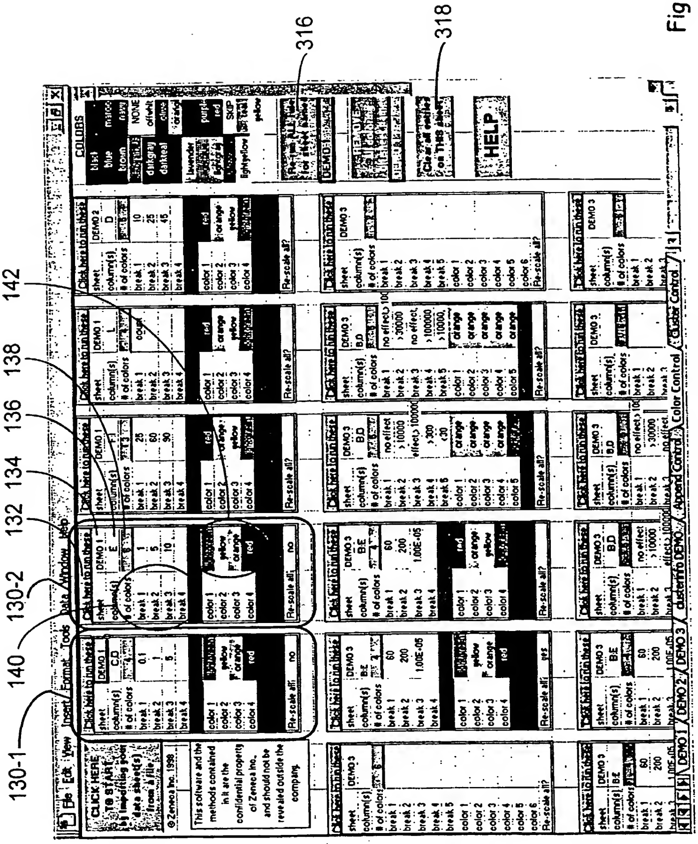


Fig. 4A

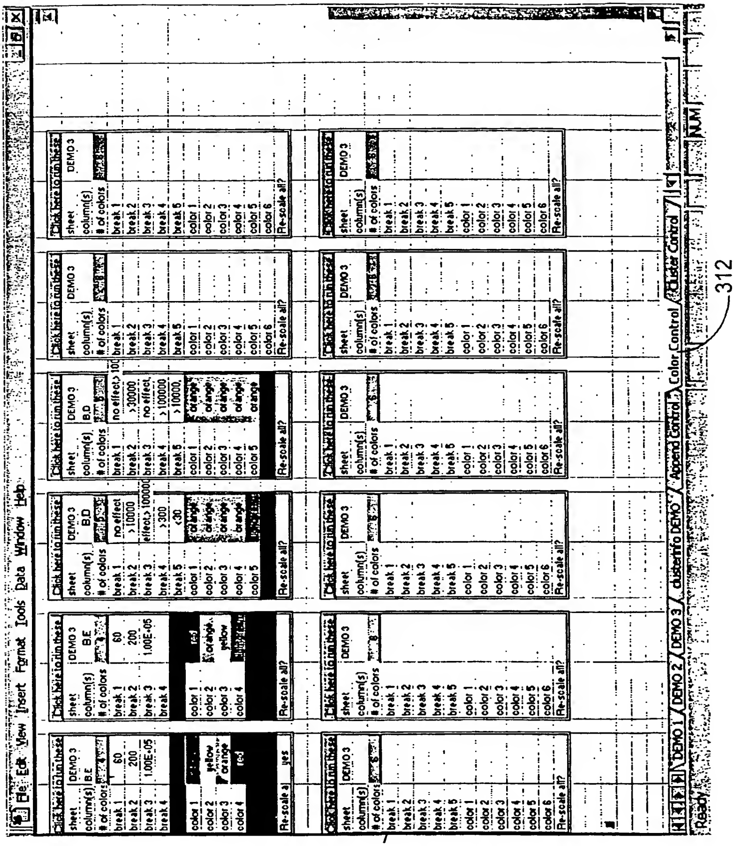

File Edit View Insert Format Tools Data Window Help
Click here to run these
sheet
column(s)
# of colors
break 1
break 2
break 3
break 4
break 5
color 1
color 2
color 3
color 4
color 5
color 6
Re-scale all?
DEMO 3
B.E
B.D
60
200
1.00E-05
no effect
>10000
>300
<30
>30000
>100000
>10000
yellow
orange
red
yes
DEMO 1 / DEMO 2 / DEMO 3 / clusterInfo DEMO / Append Control / Color Control / Cluster Control
Ready
NUM
312

Fig. 4B

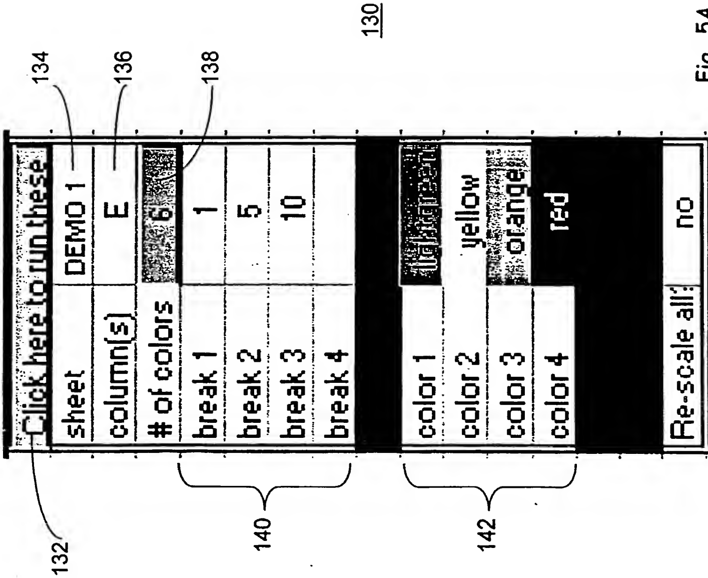

Click here to run these
sheet
DEMO 1
column(s)
E
# of colors
6
break 1
1
break 2
5
break 3
10
break 4
color 1
color 2
yellow
color 3
orange
color 4
red
Re-scale all:
no
130
132
134
136
138
140
142

Fig. 5A

10/048022

130-1

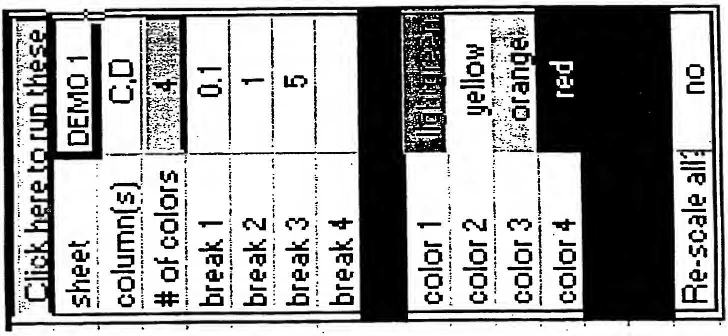


Fig. 5B

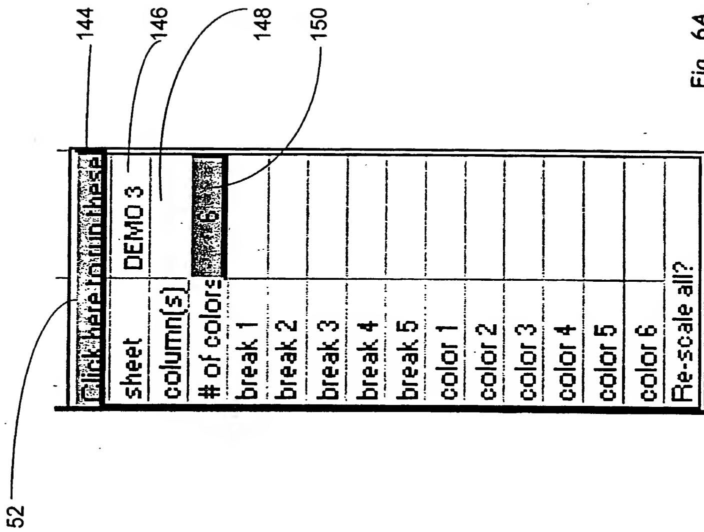

144
146
148
150
152
sheet
DEMO 3
column(s)
# of colors
6
break 1
break 2
break 3
break 4
break 5
color 1
color 2
color 3
color 4
color 5
color 6
Re-scale all?

Fig. 6A

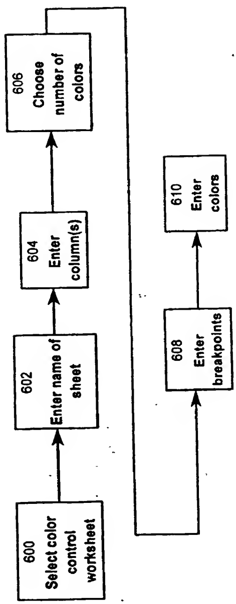
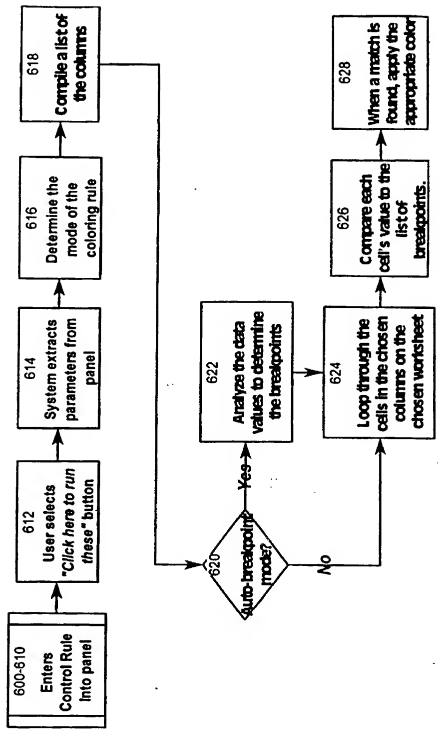

600
Select color
control
worksheet
602
Enter name of
sheet
604
Enter
column(s)
606
Choose
number of
colors
608
Enter
breakpoints
610
Enter
colors

Fig. 6B

Fig. 6C


600-610
Enters Control Rule Into panel
612
User selects "Click here to run these" button
614
System extracts parameters from panel
616
Determine the mode of the coloring rule
618
Compile a list of the columns
620
Auto-breakpoint mode?
Yes
No
622
Analyze the data values to determine the breakpoints
624
Loop through the cells in the chosen columns on the chosen worksheet
626
Compare each cell's value to the list of breakpoints.
628
When a match is found, apply the appropriate color

File Edit View Insert Format Tools Data Window Help

Cmpd	Series	Test1	Test2	Test3	HTS SPA Dose-Resp % Inhib @ 3x10-6M	HTS SPA Dose-Resp % Inhib @ 1x10-6M	HTS SPA Dose-Resp % Inhib @ 3x10-7M	HTS SPA Dose-Resp % Inhib @ 1x10-7M
Cmpd01	N		23	30				
Cmpd02	N		42	5.5	41	3	22	5
Cmpd03	G		2.81	11	83	57	28	15
Cmpd04	N			30	70	25	24	29
Cmpd05	N		1.9	9.2	89	60	21	22
Cmpd06	D	8.86	6.5	3.7	71	41	13	3
Cmpd07	D	2.11	[illegible]	7.8	100	79	48	43
Cmpd08	D		[illegible]	2.6	65	28	28	38
Cmpd09	D	0.119			68	41	22	15
Cmpd10	N	0.233			61	42	24	5
Cmpd11	N	4.31			50	77	63	25
Cmpd12	H	1.5	0.24		47	25	24	3
Cmpd13	H	1.12	0.194	30	81	59	40	37
Cmpd14	H	0.26	0.41		39	23	4	12
Cmpd15	H	0.369	0.148		99	46	46	36
Cmpd16	I		0.87	30	101	82	38	18
Cmpd17	K		0.223	30	81	64	47	24
Cmpd18	I	5.27			79	54	22	32
Cmpd19	I	0.134			71	71	23	12
Cmpd20	F		0.317		101	109	108	100
Cmpd21	K		2.21		87	70	31	13
Cmpd22	B		0.15		94	77	36	12
Cmpd23	B				96	61	36	12
Cmpd24	B		0.27		110	91	69	39
Cmpd25	B	[illegible]	1.1		105	104	75	52
Cmpd26	B	0.665			93	71	41	22
Cmpd27	B	0.111			97	79	43	23
Cmpd28	E		0.13		95	93	52	25
Cmpd29	J		0.46		68	62	12	11
Cmpd30	J	[illegible]	45		41	48	9	17
Cmpd31	N		[illegible]	5.2	5	6	21	8
Cmpd32	J	[illegible]			62	30	15	33
Cmpd33	N				112	29	75	14
Cmpd34	J	2.27	33	30	105	62	62	21
Cmpd35	J	0.63			44	28	18	3

DEMO 1 / DEMO 2 / DEMO 3 / clusterinfo DEMO / Append Control / Color Control / Cluster Control

Fig. 7A

File Edit View Insert Format Tools Data Window Help

Cmpd	Series	Test1	Test2	Test3	HTS SPA Dose-Resp % Inhib @ 3x10-6M	HTS SPA Dose-Resp % Inhib @ 1x10-6M	HTS SPA Dose-Resp % Inhib @ 3x10-7M	HTS SPA Dose-Resp % Inhib @ 1x10-7M
Cmpd32	J	[illegible]			62	30	15	33
Cmpd33	N				112	29	75	14
Cmpd34	J	[illegible]	24	30	105	62	62	21
Cmpd35	J	0.63			44	28	18	3
Cmpd36	J		0.23		93	63	42	14
Cmpd37	N	[illegible]			58	20	38	30
Cmpd38	L	[illegible]	[illegible]		90	60	51	-2
Cmpd39	F	0.56	0.41		87	73	29	15
Cmpd40	G	0.368	[illegible]		65	56	40	11
Cmpd41	G	[illegible]	0.35		66	46	28	13
Cmpd42	F	0.38	0.9		102	87	92	87
Cmpd43	H	4.45	0.13		36	25	18	12
Cmpd44	G	[illegible]	[illegible]		78	60	40	25
Cmpd45	F	0.5			111	110	104	82
Cmpd46	M	[illegible]			25	21	16	21
Cmpd47	F	[illegible]			109	104	97	80
Cmpd48	F	0.27			100	102	83	75
Cmpd49	M	[illegible]	[illegible]		71	43	31	15
Cmpd50	F	[illegible]			112	111	112	75
Cmpd51	G	[illegible]			78	70	44	27
Cmpd52	H	0.33	0.117	4.9	69	24	23	14
Cmpd53	A	[illegible]	0.18	1.6	108	102	63	27
Cmpd54	A	0.33			91	78	76	33
Cmpd55	G	9.12			61	64	60	26
Cmpd56	C	0.39			93	80	55	37
Cmpd57	A	[illegible]			101	72	42	29
Cmpd58	C	0.22			92	69	55	49

DEMO 1 / DEMO 2 / DEMO 3 / clusterInfo DEMO / Append Control / Color Control / Cluster Control

Fig. 7B

File Edit View Insert Format Tools Data Window Help

Cmpd	Series	Test1	Test2	Test3	HTS SPA Dose-Resp % Inhib @ 3x10-6M	HTS SPA Dose-Resp % Inhib @ 1x10-6M	HTS SPA Dose-Resp % Inhib @ 3x10-7M	HTS SPA Dose-Resp % Inhib @ 1x10-7M
Cmpd01	N		23	30				
Cmpd02	N		42	6.5	41	3	22	5
Cmpd03	G		2.61	11	83	57	28	15
Cmpd04	N			30	70	25	24	29
Cmpd05	N		1.8	8.2	89	60	21	22
Cmpd06	D	8.86	6.5	3.7	71	41	13	3
Cmpd07	D	0.11	[illegible]	7.8	[illegible]	79	48	43
Cmpd08	D		[illegible]	2.6	65	29	26	38
Cmpd09	D	0.119			68	41	22	15
Cmpd10	N	0.233			61	42	24	5
Cmpd11	N	4.31			60	77	63	25
Cmpd12	H	1.3	0.24		47	25	24	3
Cmpd13	H	1.17	0.194	30	81	59	40	37
Cmpd14	H	0.26	0.41		39	23	4	12
Cmpd15	H	0.369	0.148		[illegible]	46	46	36
Cmpd16	I		0.87	30	[illegible]	82	38	18
Cmpd17	K		0.223	30	81	64	47	24
Cmpd18	I	5.27			79	54	22	32
Cmpd19	I	0.134			71	71	23	12
Cmpd20	F		0.317		[illegible]	[illegible]	[illegible]	[illegible]
Cmpd21	K		2.21		87	70	31	13
Cmpd22	B		0.15		[illegible]	77	38	12
Cmpd23	B				[illegible]	61	36	12
Cmpd24	B		0.27		[illegible]	[illegible]	69	38
Cmpd25	B	[illegible]	[illegible]		[illegible]	[illegible]	75	52
Cmpd26	B	0.665			[illegible]	71	41	22
Cmpd27	B	0.111			[illegible]	79	43	23
Cmpd28	E		0.13		[illegible]	[illegible]	82	25
Cmpd29	J		0.46		68	62	12	11
Cmpd30	J	[illegible]	45		[illegible]	48	9	17
Cmpd31	N		[illegible]	[illegible]	5	6	21	8
Cmpd32	J	[illegible]			62	30	15	33
Cmpd33	N				[illegible]	28	75	14

DEMO 1 / DEMO 2 / DEMO 3 / clusterInfo DEMO / Append Control / Color Control / Cluster Control

Ready NUM

Fig. 8A

File Edit View Insert Format Tools Data Window Help

Cmpd	Series	Test1	Test2	Test3	HTS SPA Dose-Resp % Inhib @ 3x10-6M	HTS SPA Dose-Resp % Inhib @ 1x10-6M	HTS SPA Dose-Resp % Inhib @ 3x10-7M	HTS SPA Dose-Resp % Inhib @ 1x10-7M
Cmpd34	J	2.27	34	30	[illegible]	62	62	21
Cmpd35	J	0.63			[illegible]	28	18	3
Cmpd36	J		0.23		[illegible]	63	42	14
Cmpd37	N	12.3			[illegible]	30	38	30
Cmpd38	L	[illegible]			90	60	61	-2
Cmpd39	F	0.56	0.41		87	73	29	15
Cmpd40	G	0.368	1.043		65	[illegible]	40	11
Cmpd41	G	[illegible]	0.35		66	46	28	13
Cmpd42	F	0.38	0.9		[illegible]	87	[illegible]	87
Cmpd43	H	4.46	0.13		[illegible]	35	18	12
Cmpd44	G	[illegible]	[illegible]		78	60	40	25
Cmpd45	F	0.5			[illegible]	[illegible]	[illegible]	82
Cmpd46	M	1.14			25	21	16	21
Cmpd47	F	[illegible]			[illegible]	[illegible]	[illegible]	80
Cmpd48	F	0.27			[illegible]	[illegible]	83	75
Cmpd49	M	[illegible]			71	43	31	15
Cmpd50	F	[illegible]			[illegible]	[illegible]	[illegible]	75
Cmpd51	G	[illegible]			78	70	44	27
Cmpd52	H	0.33	0.117	4.9	69	24	23	14
Cmpd53	A	[illegible]	0.18	1.6	[illegible]	[illegible]	63	27
Cmpd54	A	0.33			[illegible]	78	76	33
Cmpd55	G	9.12			61	64	60	26
Cmpd56	C	0.39			[illegible]	80	85	37
Cmpd57	A	[illegible]			[illegible]	72	42	29
Cmpd58	C	0.22			[illegible]	69	85	49

DEMO 1 / DEMO 2 / DEMO 3 / clusterinfo DEMO / Append Control / Color Control / Cluster Control

Ready NUM

Fig. 8B

File Edit View Insert Format Tools Data Window Help

mixture	acid	amine group	activity @ 1 μM
E1_A	E1	A	47
E1_B	E1	B	58
E1_C	E1	C	40
E1_D	E1	D	52
E2_A	E2	A	7
E2_B	E2	B	69
E2_C	E2	C	40
E2_D	E2	D	17
E3_A	E3	A	17
E3_B	E3	B	22
E3_C	E3	C	20
E3_D	E3	D	14
E4_A	E4	A	22
E4_B	E4	B	17
E4_C	E4	C	-27
E4_D	E4	D	12
E5_A	E5	A	-3
E5_B	E5	B	5
E5_C	E5	C	28
E5_D	E5	D	10
E6_A	E6	A	5
E6_B	E6	B	18
E6_C	E6	C	10
E6_D	E6	D	17
E7_A	E7	A	74
E7_B	E7	B	26
E7_C	E7	C	42
E7_D	E7	D	52
F1_A	F1	A	42
F1_B	F1	B	34
F1_C	F1	C	57
F1_D	F1	D	41
F2_A	F2	A	32
F2_B	F2	B	61
F2_C	F2	C	72
F2_D	F2	D	53
F3_A	F3	A	14
F3_B	F3	B	38
F3_C	F3	C	33
F3_D	F3	D	42
F4_A	F4	A	-41
F4_B	F4	B	9
F4_C	F4	C	18

DEMO 1 / DEMO 2 / DEMO 3 / ClusterInfo DEMO / Append Control / Color Control / Cluster Control

Fig. 9A

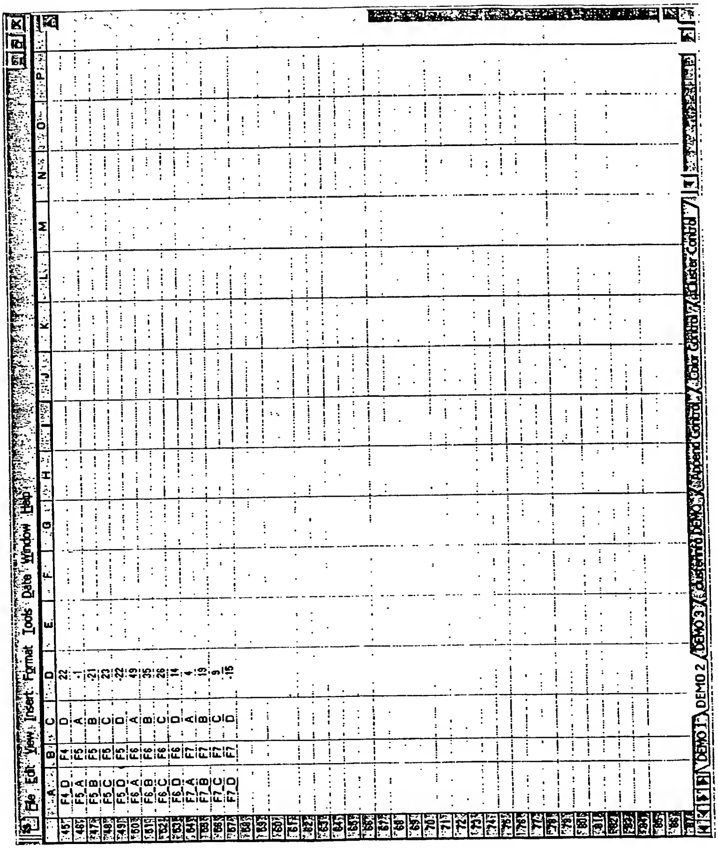
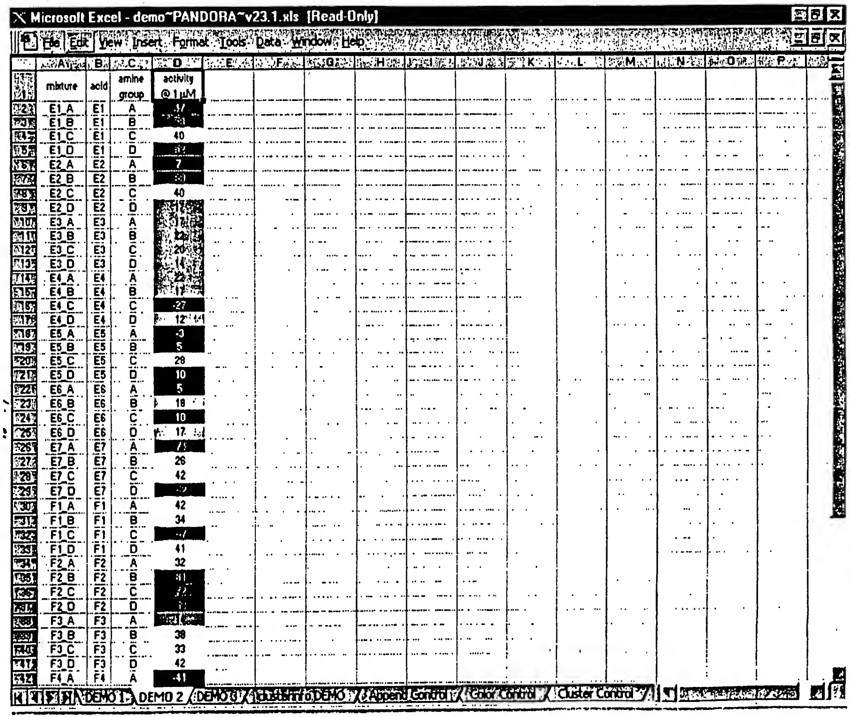

File Edit View Insert Format Tools Data Window Help
DEMO 1
DEMO 2
DEMO3
Append Control
Color Control
Cluster Control

Fig. 9B



mixture	acid	amine group	activity @ 1 μM
E1_A	E1	A	[illegible]
E1_B	E1	B	[illegible]
E1_C	E1	C	40
E1_D	E1	D	[illegible]
E2_A	E2	A	7
E2_B	E2	B	[illegible]
E2_C	E2	C	40
E2_D	E2	D	[illegible]
E3_A	E3	A	[illegible]
E3_B	E3	B	22
E3_C	E3	C	20
E3_D	E3	D	14
E4_A	E4	A	22
E4_B	E4	B	17
E4_C	E4	C	-27
E4_D	E4	D	12
E5_A	E5	A	-3
E5_B	E5	B	5
E5_C	E5	C	28
E5_D	E5	D	10
E6_A	E6	A	5
E6_B	E6	B	18
E6_C	E6	C	10
E6_D	E6	D	17
E7_A	E7	A	[illegible]
E7_B	E7	B	26
E7_C	E7	C	42
E7_D	E7	D	[illegible]
F1_A	F1	A	42
F1_B	F1	B	34
F1_C	F1	C	[illegible]
F1_D	F1	D	41
F2_A	F2	A	32
F2_B	F2	B	[illegible]
F2_C	F2	C	[illegible]
F2_D	F2	D	[illegible]
F3_A	F3	A	[illegible]
F3_B	F3	B	38
F3_C	F3	C	33
F3_D	F3	D	42
F4_A	F4	A	-41

Fig. 10A

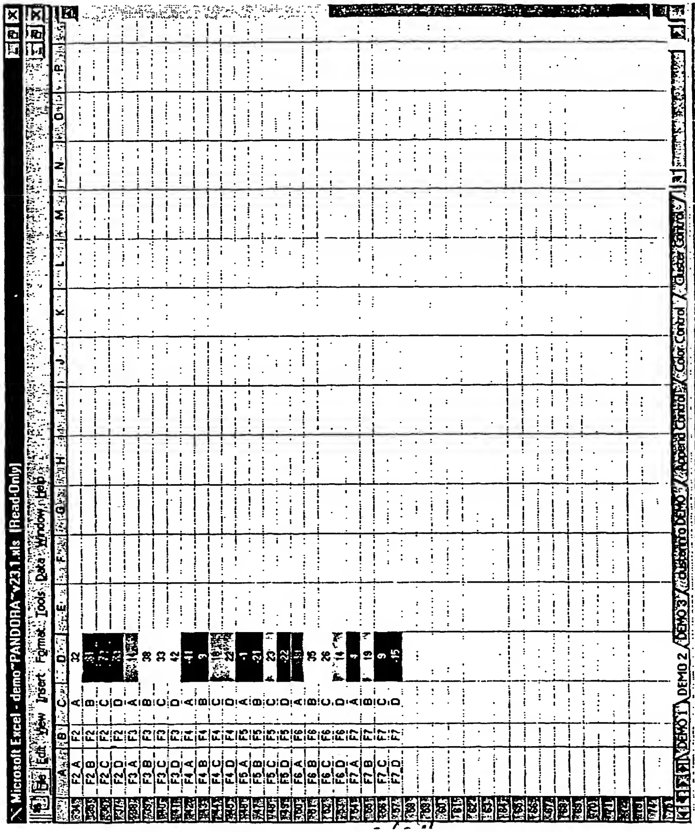
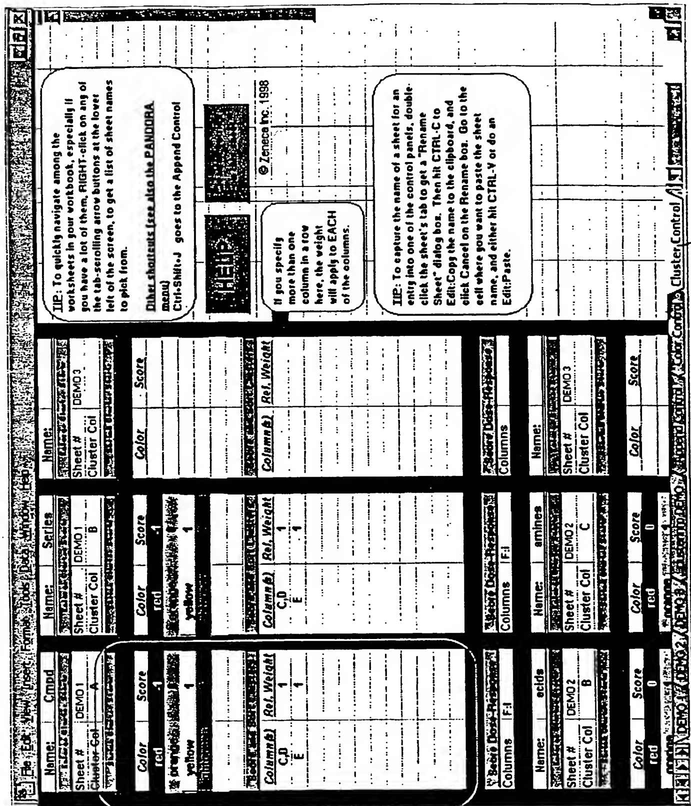

Microsoft Excel - demo~PANDORA~v23.1.xls [Read-Only]
File Edit View Insert Format Tools Data Window Help
DEMO 1
DEMO 2
DEMO 3
cluster to DEMO
Append Control
Color Control
cluster Control

Fig. 10B



1100

314

Fig. 11A

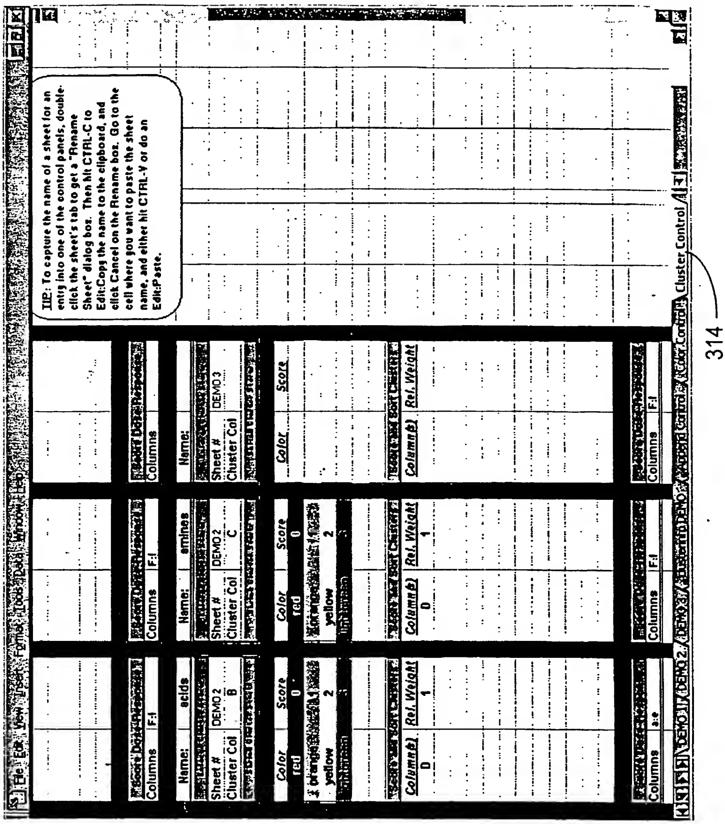

TIP: To capture the name of a sheet for an entry into one of the control panels, double-click the sheet's tab to get a "Rename Sheet" dialog box. Then hit CTRL-C to Edit:Copy the name to the clipboard, and click Cancel on the Rename box. Go to the cell where you want to paste the sheet name, and either hit CTRL-V or do an Edit:Paste.
Cluster Control
314

Fig. 11B

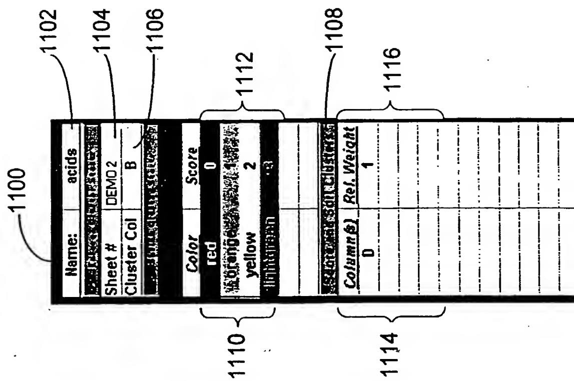

1100
1102
1104
1106
1108
1110
1112
1114
1116
Name:
acids
Sheet #
DEMO2
Cluster Col
B
Color
Score
red
0
orange
yellow
2
lightgreen
3
Column(s)
Rel. Weight
D
1

Fig. 11C

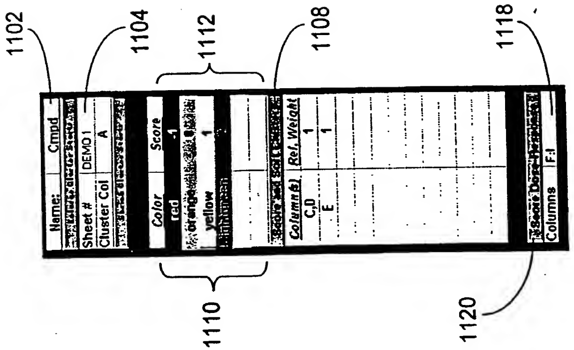

1102
1104
1112
1108
1118
1110
1120
Name:
Cmpd
Sheet #
DEMO1
Cluster Col
A
Color
Score
red
-1
orange
yellow
1
Column(s)
Ref. Weight
C,D
1
E
1
Columns
F:I

Fig. 11D

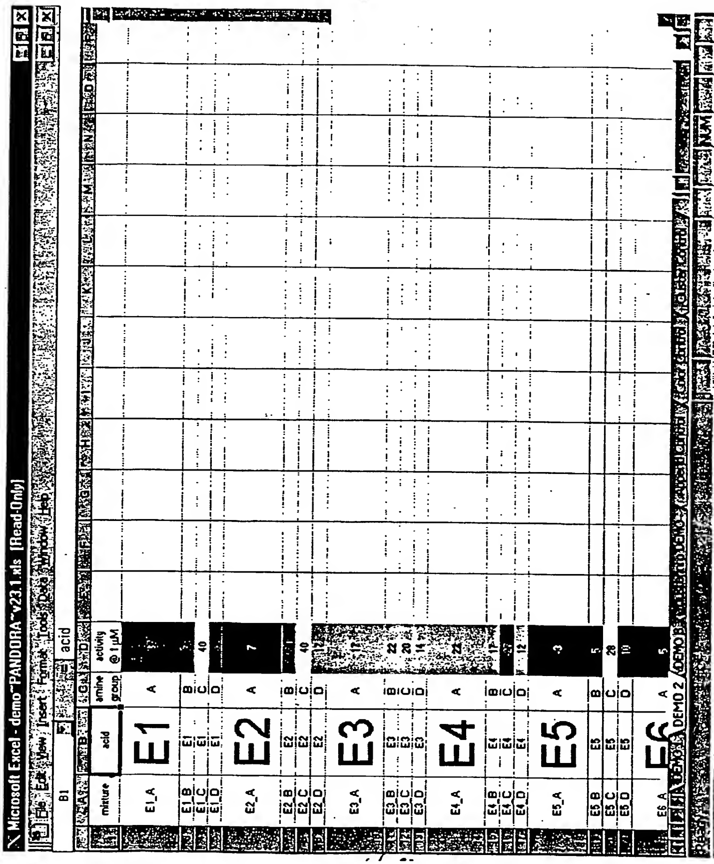
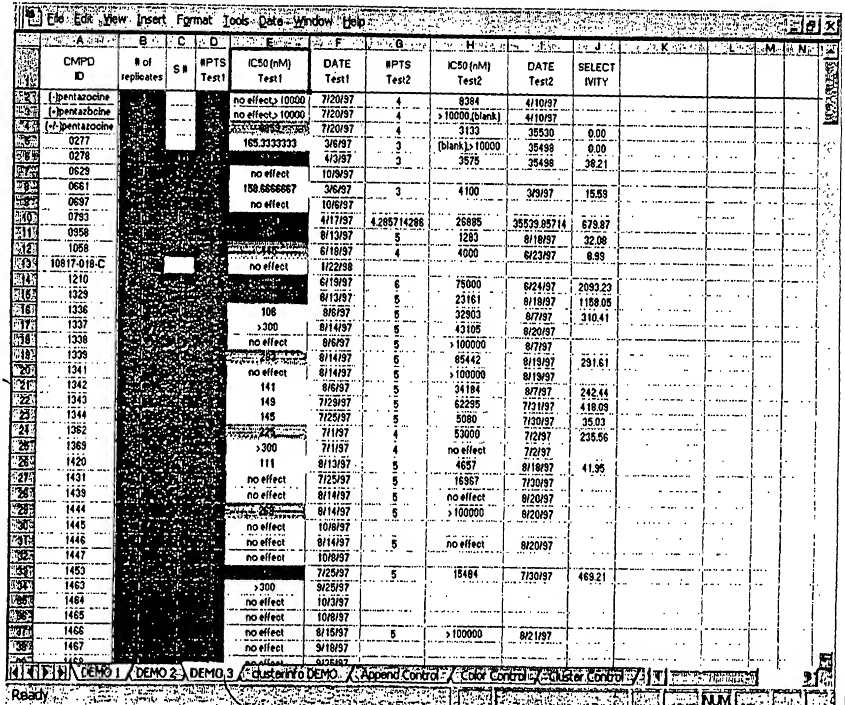

Microsoft Excel - demo~PANDORA~v23.1.xls [Read-Only]
File Edit View Insert Format Tools Data Window Help
B1
acid
mixture
acid
amine group
activity @1 µM
E1_A
E1
E2_A
E2
E3_A
E3
E4_A
E4
E5_A
E5
E6_A
DEMO 2
DEMO B
NUM

Fig. 12



	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1	CMPD ID	# of replicates	S #	#PTS Test1	IC50 (nM) Test1	DATE Test1	#PTS Test2	IC50 (nM) Test2	DATE Test2	SELECTIVITY				
2	(-)pentazocine				no effect,> 10000	7/20/97	4	8384	4/10/97					
3	(+)pentazocine				no effect,> 10000	7/20/97	4	> 10000,(blank)	4/10/97					
4	(+/-)pentazocine				[illegible]	7/20/97	4	3133	35530	0.00				
5	0277				165.3333333	3/6/97	3	(blank),> 10000	35498	0.00				
6	0278					4/3/97	3	3575	35498	38.21				
7	0629				no effect	10/9/97								
8	0661				158.6666667	3/6/97	3	4100	3/9/97	15.59				
9	0697				no effect	10/6/97								
10	0793					4/17/97	4.285714286	26885	35539.85714	679.87				
11	0958					8/13/97	5	1283	8/18/97	32.08				
12	1058				[illegible]	6/18/97	4	4000	6/23/97	8.99				
13	10817-018-C				no effect	1/22/98								
14	1210					6/19/97	6	75000	6/24/97	2093.23				
15	1329					8/13/97	5	23161	8/18/97	1158.05				
16	1336				106	8/6/97	5	32903	8/7/97	310.41				
17	1337				>300	8/14/97	5	43105	8/20/97					
18	1338				no effect	8/6/97	5	>100000	8/7/97					
19	1339				[illegible]	8/14/97	5	85442	8/19/97	291.61				
20	1341				no effect	8/14/97	5	>100000	8/19/97					
21	1342				141	8/6/97	5	34184	8/7/97	242.44				
22	1343				149	7/29/97	5	62295	7/31/97	418.09				
23	1344				145	7/25/97	5	5080	7/30/97	35.03				
24	1362				[illegible]	7/1/97	4	53000	7/2/97	235.56				
25	1369				>300	7/1/97	4	no effect	7/2/97					
26	1420				111	8/13/97	5	4657	8/18/97	41.95				
27	1431				no effect	7/25/97	5	16967	7/30/97					
28	1439				no effect	8/14/97	5	no effect	8/20/97					
29	1444				[illegible]	8/14/97	5	>100000	8/20/97					
30	1445				no effect	10/8/97								
31	1446				no effect	8/14/97	5	no effect	8/20/97					
32	1447				no effect	10/8/97								
33	1453					7/25/97	5	15484	7/30/97	469.21				
34	1463				>300	9/25/97								
35	1464				no effect	10/3/97								
36	1465				no effect	10/8/97								
37	1466				no effect	8/15/97	5	>100000	8/21/97					
38	1467				no effect	9/18/97								
39	[illegible]				no effect	9/25/97								

306

Fig. 13A

File Edit View Insert Format Tools Data Window Help

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1	CMPD ID	# of replicates	S #	#PTS Test1	IC50 (nM) Test1	DATE Test1	#PTS Test2	IC50 (nM) Test2	DATE Test2	SELECTIVITY				
294	5533	[redacted]	[redacted]	[redacted]	134	6/20/97	4	11000	6/25/97	82.09				
295	6281	[redacted]	[redacted]	[redacted]	[redacted]	6/20/97	5	6000	6/25/97	171.43				
296	6478	[redacted]	[redacted]	[redacted]	[redacted]	9/17/97	5	2660	9/16/97	49.26				
297	6573	[redacted]	[redacted]	[redacted]	>300	9/4/97	5	2486	9/11/97					
298	6741	[redacted]	[redacted]	[redacted]	[redacted]	9/17/97	5	1330	9/16/97	23.75				
299	6930	[redacted]	[redacted]	[redacted]	[redacted]	6/18/97	5	10000	6/23/97	1000.00				
300	7077	[redacted]	[redacted]	[redacted]	>300	6/18/97	4	>100000	6/23/97					
301	7339	[redacted]	[redacted]	[redacted]	no effect	10/6/97								
302	7366	[redacted]	[redacted]	[redacted]	>10000	6/12/97	4	419	4/10/97					
303	7781	[redacted]	[redacted]	[redacted]	82	6/26/97	5	19000	7/3/97	231.71				
304	7946	[redacted]	[redacted]	[redacted]	63	6/12/97	5	200	1/27/97	3.17				
305	8374	[redacted]	[redacted]	[redacted]	185	7/27/97	5	2706	7/16/97	14.63				
306	8437	[redacted]	[redacted]	[redacted]	no effect	9/25/97								
307	8503	[redacted]	[redacted]	[redacted]	165	8/15/97	5	>100000	8/21/97					
308	8516	[redacted]	[redacted]	[redacted]	[redacted]	8/13/97	5	1872	8/18/97	31.73				
309	8517	[redacted]	[redacted]	[redacted]	[redacted]	8/13/97	5	2836	8/18/97	72.72				
310	8671	[redacted]	[redacted]	[redacted]	>300	7/29/97	5	39852	7/31/97					
311	8826	[redacted]	[redacted]	[redacted]	>300	9/18/97	5	no effect	9/16/97					
312	8857	[redacted]	[redacted]	[redacted]	[illegible]	9/4/97	5	3233	9/9/97	15.18				
313	8858	[redacted]	[redacted]	[redacted]	no effect	9/4/97	5	9480	9/9/97					
314	8860	[redacted]	[redacted]	[redacted]	no effect	9/4/97	5	10830	9/9/97					
315	9116	[redacted]	[redacted]	[redacted]	106	7/28/97	5	16000	7/10/97	150.94				
316	9176	[redacted]	[redacted]	[redacted]	[redacted]	8/13/97	5	2013	8/18/97	45.75				
317	9177	[redacted]	[redacted]	[redacted]	[redacted]	8/13/97	5	1168	8/18/97	83.43				
318	9202	[redacted]	[redacted]	[redacted]	no effect	9/3/97	5	3143	9/9/97					
319	9386	[redacted]	[redacted]	[redacted]	[redacted]	1/22/98				0.00				
320	9657	[redacted]	[redacted]	[redacted]	>300	10/3/97								
321	9751	[redacted]	[redacted]	[redacted]	[redacted]	11/14/97	5	1880	11/19/97	82.53				
322	9940	[redacted]	[redacted]	[redacted]	no effect	10/8/97								
323	DHEA-S	[redacted]		[redacted]	no effect	8/24/97	5	no effect,(blank)	8/20/97					
324	DTG	[redacted]		[redacted]	>10000	3/5/97	5	21360	2/2/97					
325	Haloperidol	[redacted]		[redacted]	[illegible]	6/12/97	5	800	2/5/97	1.11				
326	PPBP	[redacted]		[redacted]	[redacted]	9/17/97	5	3570	9/16/97	123.10				
327	PPP	[redacted]		[redacted]	>10000	3/7/97	5	75170	2/6/97					
328	pregnenolone	[redacted]		[redacted]	no effect,>10000	8/24/97	5	no effect,(blank)	8/20/97					
329	progesterone	[redacted]		[redacted]	[illegible]	8/24/97	5	(blank),no effect	8/20/97	0.00				
330														

DEMO 1 / DEMO 2 / DEMO 3 / clusterInfo DEMO / Append Control / Color Control / Cluster Control /

Ready NUM

306

Fig. 13B

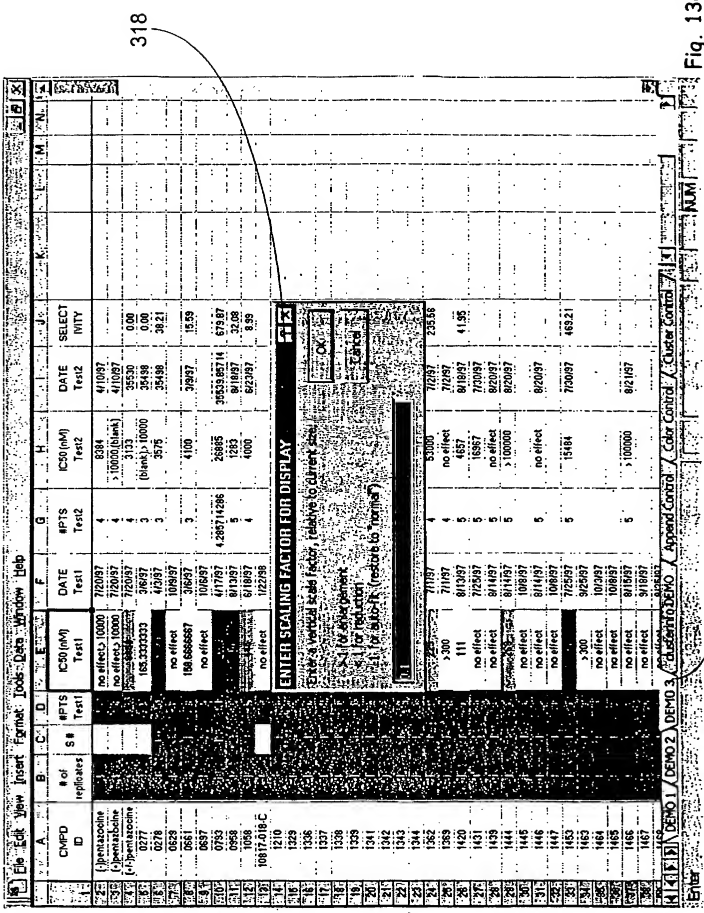

318
ENTER SCALING FACTOR FOR DISPLAY
OK
Cancel
306
DEMO 1
DEMO 2
DEMO 3
Append Control
Color Control
Cluster Control
NUM
Enter

Fig. 13C

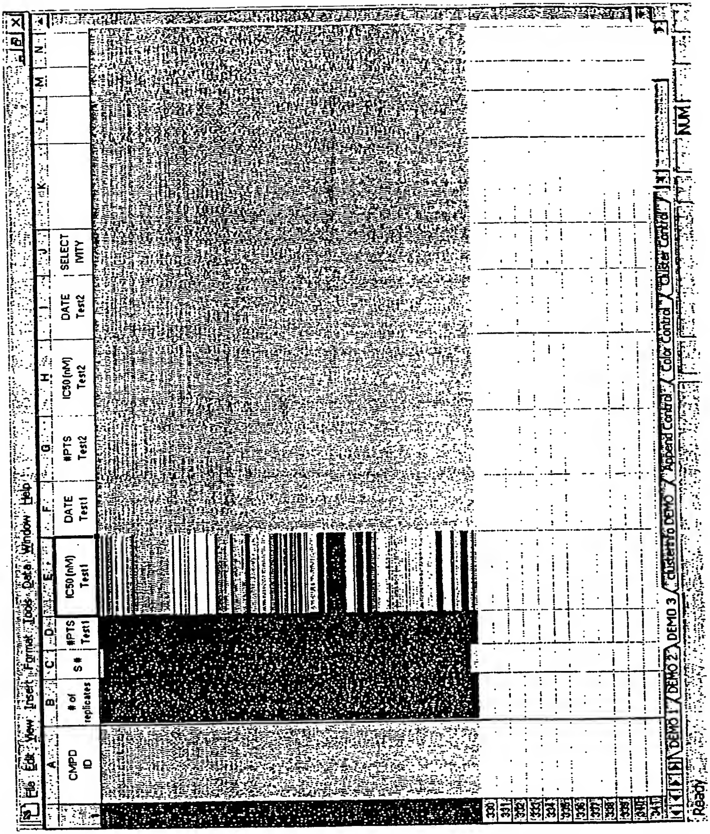

File Edit View Insert Format Tools Data Window Help
A
B
C
D
E
F
G
H
I
J
K
L
M
N
CMPD ID
# of replicates
S #
#PTS Test1
IC50 (nM) Test1
DATE Test1
#PTS Test2
IC50 (nM) Test2
DATE Test2
SELECT IVITY
330
331
332
333
334
335
336
337
338
339
340
341
DEMO 1
DEMO 2
DEMO 3
Append Control
Color Control
Cluster Control
Ready
NUM

Fig. 13D

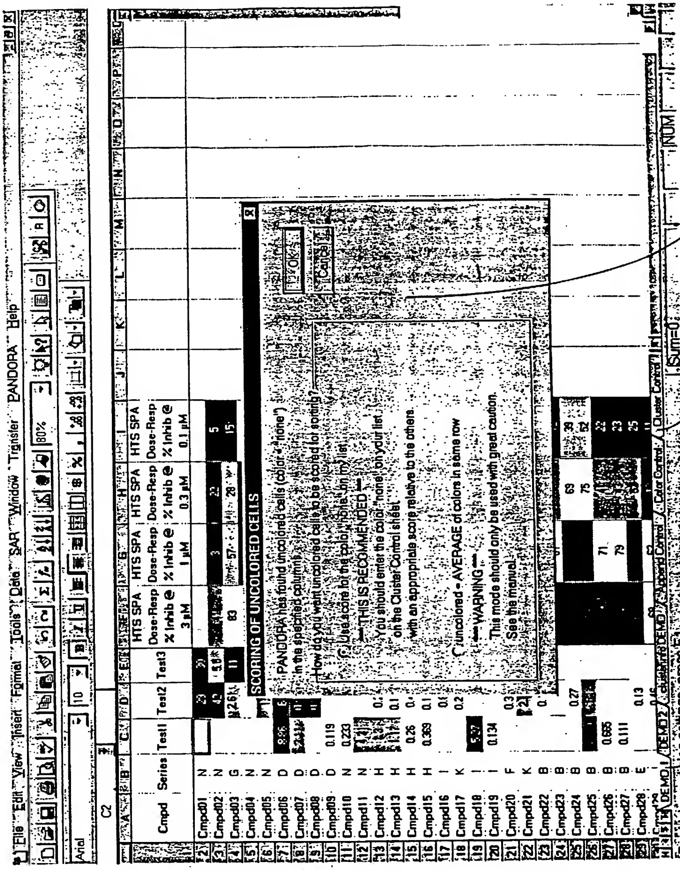

File Edit View Insert Format Tools Data SAR Window Transfer PANDORA Help
SCORING OF UNCOLORED CELLS
PANDORA has found uncolored cells (color = "none")
in the specified columns.
How do you want uncolored cells to be scored for sorting?
Use score for the color "none" on my list
— THIS IS RECOMMENDED —
You should enter the color "none" on your list
on the Cluster Control sheet
with an appropriate score relative to the others.
uncolored = AVERAGE of colors in same row
— WARNING —
This mode should only be used with great caution.
See the manual.
OK
Cancel
For Help on dialog settings, press F1
1402
314
302

Fig. 14A

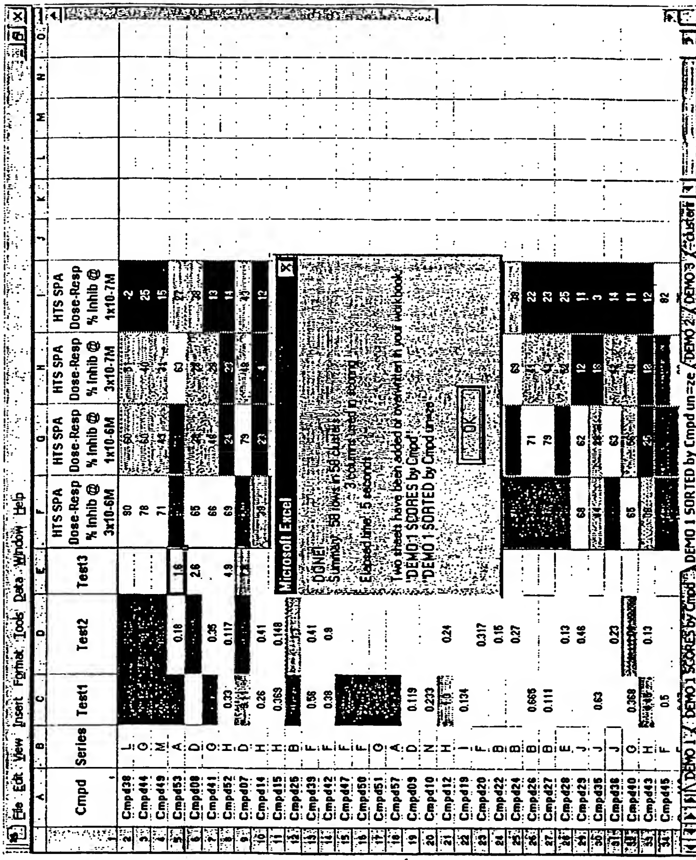

File Edit View Insert Format Tools Data Window Help
Cmpd
Series
Test1
Test2
Test3
HTS SPA Dose-Resp % Inhib @ 3x10-6M
HTS SPA Dose-Resp % Inhib @ 1x10-6M
HTS SPA Dose-Resp % Inhib @ 3x10-7M
HTS SPA Dose-Resp % Inhib @ 1x10-7M
Microsoft Excel
DONE!
Summary: 58 rows in 58 clusters
3 columns used in scoring
Elapsed time: 5 seconds
Two sheets have been added or overwritten in your workbook
'DEMO1 SCORES by Cmpd'
'DEMO1 SORTED by Cmpd un=ze
OK
DEMO1
DEMO1 SCORES by Cmpd
DEMO1 SORTED by Cmpd un=ze
DEMO2
DEMO3
clusters
NUM

Fig. 14B

File Edit View Insert Format Tools Data Window Help

	A	B	C	D	E
1	cluster label	# of cmpds	score max. 100 (uncolored = zero)	[illegible]	<-- Scoring of sheet "DEMO 1" using parameter set "Cmpd"
2	Cmpd38	1	67	100	
3	Cmpd44	1	67	100	
4	Cmpd49	1	67	100	
5	Cmpd53	1	67	57	
6	Cmpd08	1	50	[illegible]	
7	Cmpd41	1	50	[illegible]	
8	Cmpd52	1	50	50	
9	Cmpd07	1	33	[illegible]	
10	Cmpd14	1	33	[illegible]	
11	Cmpd15	1	33	[illegible]	
12	Cmpd25	1	33	[illegible]	
13	Cmpd39	1	33	[illegible]	
14	Cmpd42	1	33	[illegible]	
15	Cmpd47	1	33	[illegible]	
16	Cmpd50	1	33	[illegible]	
17	Cmpd51	1	33	[illegible]	
18	Cmpd57	1	33	[illegible]	
19	Cmpd09	1	17	[illegible]	
20	Cmpd10	1	17	[illegible]	
21	Cmpd12	1	17	[illegible]	
22	Cmpd19	1	17	[illegible]	
23	Cmpd20	1	17	[illegible]	
24	Cmpd22	1	17	[illegible]	
25	Cmpd24	1	17	[illegible]	
26	Cmpd26	1	17	[illegible]	
27	Cmpd27	1	17	[illegible]	
28	Cmpd28	1	17	[illegible]	
29	Cmpd29	1	17	[illegible]	
30	Cmpd35	1	17	[illegible]	
31	Cmpd36	1	17	[illegible]	
32	Cmpd40	1	17	[illegible]	
33	Cmpd43	1	17	[illegible]	
34	Cmpd45	1	17	[illegible]	
35	Cmpd48	1	17	[illegible]	
36	Cmpd54	1	17	[illegible]	
37	Cmpd56	1	17	[illegible]	

DEMO 1 / DEMO 1 SCORES by Cmpd / DEMO 1 SORTED by Cmpd un=26 / DEMO 2 / DEMO 3 / cluster

Ready NUM

Fig. 14C

File Edit View Insert Format Tools Data Window Help

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
30	Cmpd35	1	17	[illegible]												
31	Cmpd36	1	17	[illegible]												
32	Cmpd40	1	17	[illegible]												
33	Cmpd43	1	17	[illegible]												
34	Cmpd45	1	17	[illegible]												
35	Cmpd48	1	17	[illegible]												
36	Cmpd54	1	17	[illegible]												
37	Cmpd56	1	17	[illegible]												
38	Cmpd58	1	17	[illegible]												
39	Cmpd05	1	0	[illegible]												
40	Cmpd11	1	0	[illegible]												
41	Cmpd13	1	0	[illegible]												
42	Cmpd16	1	0	[illegible]												
43	Cmpd17	1	0	[illegible]												
44	Cmpd21	1	0	[illegible]												
45	Cmpd23	1	0	[illegible]												
46	Cmpd31	1	0	[illegible]												
47	Cmpd32	1	0	[illegible]												
48	Cmpd33	1	0	[illegible]												
49	Cmpd46	1	0	[illegible]												
50	Cmpd02	1	-33	[illegible]												
51	Cmpd03	1	-33	[illegible]												
52	Cmpd04	1	-33	[illegible]												
53	Cmpd06	1	-33	[illegible]												
54	Cmpd18	1	-33	[illegible]												
55	Cmpd30	1	-33	[illegible]												
56	Cmpd37	1	-33	[illegible]												
57	Cmpd55	1	-33	[illegible]												
58	Cmpd01	1	-67	[illegible]												
59	Cmpd34	1	-67	[illegible]												
60																
61																
62																
63																
64																
65																
66																
67																
68																
69																
70																
71																

DEMO 1 / DEMO 1 SCORES by Cmpd / DEMO 1 SORTED by Cmpd un=ze / DEMO 2 / DEMO 3 / cluster

Fig. 14D

File Edit View Insert Format Tools Data Window Help

cluster label	# of cmpds	score max. 100 (uncolored = zero)	score max. 100 (uncolored = average)	<-- Scoring of sheet "DEMO 2" using parameter set "acids"
E1	4	92	92	
F2	4	92	92	
E7	4	83	83	
F1	4	75	75	
F6	4	67	67	
F3	4	58	58	
E2	4	50	50	
E3	4	33	33	
E4	4	25	25	
E5	4	17	17	
E6	4	17	17	
F4	4	17	17	
F5	4	8	8	
F7	4	8	8	

DEMO 2 / DEMO 2 SCORES by acids / DEMO 2 SORTED by acids / DEMO 3 / clusterinfo DEMO / Appel

Fig. 15A

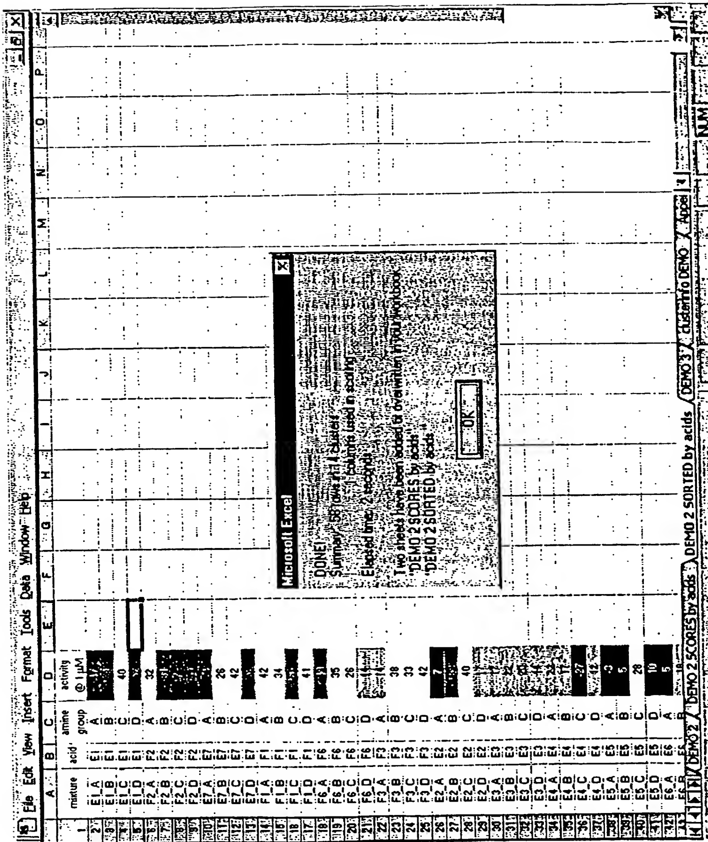

File Edit View Insert Format Tools Data Window Help
mixture
acid
amine group
activity @ 1 µM
Microsoft Excel
DONE!
Elapsed time: 2 seconds
Two sheets have been added (& overwritten) in your workbook:
"DEMO 2 SCORES by acids"
"DEMO 2 SORTED by acids"
OK
DEMO 2
DEMO 2 SCORES by acids
DEMO 2 SORTED by acids
DEMO 3
NUM

Fig. 15B

	A	B	C	D	E
1	Cmpd	HTS SPA Dose-Resp % Inhib @ 3x10-6M	HTS SPA Dose-Resp % Inhib @ 1x10-6M	HTS SPA Dose-Resp % Inhib @ 3x10-7M	HTS SPA Dose-Resp % Inhib @ 1x10-7M
2	Cmpd01	90	22	16	19
3	Cmpd02	41	3	22	5
4	Cmpd03	83	57	28	15
5	Cmpd04	70	25	24	29
6	Cmpd05	89	60	21	22
7	Cmpd06	71	41	13	3
8	Cmpd07	100	79	48	43
9	Cmpd08	65	28	28	38
10	Cmpd09	68	41	22	15
11	Cmpd10	61	42	24	5
12	Cmpd11	50	77	63	25
13	Cmpd12	47	25	24	3
14	Cmpd13	81	59	40	37
15	Cmpd14	39	23	4	12
16	Cmpd15	99	46	46	36
17	Cmpd16	101	[illegible]	38	18
18	Cmpd17	91	64	47	24
19	Cmpd18	79	54	22	32
20	Cmpd19	71	71	23	12
21	Cmpd20	101	109	109	[illegible]

Figure 16A

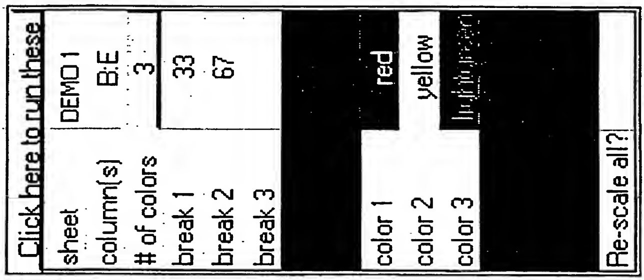

Click here to run these
sheet
DEMO 1
column(s)
B:E
# of colors
3
break 1
33
break 2
67
break 3
color 1
red
color 2
yellow
color 3
Re-scale all?

Figure 16B

1	A Cmpd	B HTS SPA Dose-Resp % Inhib @ 3x10-6M 3.00e-06	C HTS SPA Dose-Resp % Inhib @ 1x10-6M 1.00e-06	D HTS SPA Dose-Resp % Inhib @ 3x10-7M 3.00e-07	E HTS SPA Dose-Resp % Inhib @ 1x10-7M 1.00e-07
2	Cmpd20	101	[illegible]	[illegible]	[illegible]
3	Cmpd07	100	[illegible]	48	43
4	Cmpd13	91	59	40	37
5	Cmpd15	99	46	46	36
6	Cmpd16	101	[illegible]	38	18
7	Cmpd17	91	64	47	24
8	Cmpd03	89	57	28	15
9	Cmpd05	99	60	21	22
10	Cmpd06	71	41	13	3
11	Cmpd09	69	41	22	15
12	Cmpd11	50	[illegible]	63	25
13	Cmpd18	70	54	22	32
14	Cmpd19	71	[illegible]	23	12
15	Cmpd10	61	42	24	5
16	Cmpd01	90	22	16	19
17	Cmpd04	70	25	24	29
18	Cmpd02	41	3	22	5
19	Cmpd08	65	28	28	38
20	Cmpd12	47	25	24	3
21	Cmpd14	39	23	4	12

1	A Cmpd	F D-R -iveness score (0 to 100) by Cmpd	G D-R activity score (0 to 100) by Cmpd	H D-R composite score (0 to 100) by Cmpd
2	Cmpd20	75	100	100
3	Cmpd07	83	77	79
4	Cmpd13	83	70	75
5	Cmpd15	83	70	75
6	Cmpd16	92	50	70
7	Cmpd17	92	43	67
8	Cmpd03	92	23	57
9	Cmpd05	92	23	57
10	Cmpd06	92	23	57
11	Cmpd09	92	23	57
12	Cmpd11	67	47	57
13	Cmpd18	92	23	57
14	Cmpd19	83	30	56
15	Cmpd10	83	20	51
16	Cmpd01	83	10	46
17	Cmpd04	83	10	46
18	Cmpd02	83	7	45
19	Cmpd08	58	33	45
20	Cmpd12	83	7	45
21	Cmpd14	83	7	45

Fig. 16C

	A	B	C	D	E	F	G	H
1	Cmpd	HTS SPA Dose-Resp % Inhib @ 3x10-6M 3.00e-06	HTS SPA Dose-Resp % Inhib @ 1x10-6M 1.00e-06	HTS SPA Dose-Resp % Inhib @ 3x10-7M 3.00e-07	HTS SPA Dose-Resp % Inhib @ 1x10-7M 1.00e-07	D-R -iveness score (0 to 100) by Cmpd	D-R activity score (0 to 100) by Cmpd	D-R composit score (0 to 100) by Cmpd
22	marker_7.5	99	97	90	76	75	100	100
23	marker_7.0	97	91	75	50	83	87	86
24	marker_6.5	90	76	49	24	92	50	70
25	marker_6.0	76	50	23	9	92	23	57
26	marker_5.5	49	24	9	3	83	7	45
27	marker_5.0	23	9	3	1	75	0	38

Figure 16D

	A	B	C	D	E	F	G	H	I	J
1	Cmpd	HTS SPA Dose-Resp % Inhib @ 3x10-6M 3.00e-06	HTS SPA Dose-Resp % Inhib @ 1x10-6M 1.00e-06	HTS SPA Dose-Resp % Inhib @ 3x10-7M 3.00e-07	HTS SPA Dose-Resp % Inhib @ 1x10-7M 1.00e-07	D-R -iveness score (0 to 100) by Cmpd	D-R activity score (0 to 100) by Cmpd	D-R composite score (0 to 100) by Cmpd	Interp -log IC50 by Cmpd	est IC50 µM by Cmpd
2	Cmpd20	[illegible]	[illegible]	[illegible]	100	75	100	100		<0.1
3	marker_7.5	[illegible]	[illegible]	[illegible]	[illegible]	75	100	100		
4	marker_7.0	[illegible]	[illegible]	[illegible]	50	83	87	86		
5	Cmpd07	100	[illegible]	48	43	83	77	79	6.78	0.17
6	Cmpd13	[illegible]	59	40	37	83	70	75	6.66	0.22
7	Cmpd15	[illegible]	46	46	36	83	70	75	6.66	0.22
8	Cmpd16	[illegible]	[illegible]	38	18	92	50	70	6.50	0.32
9	marker_6.5	[illegible]	[illegible]	49	24	92	50	70		
10	Cmpd17	[illegible]	64	47	24	92	43	67	6.38	0.41
11	Cmpd03	[illegible]	57	28	15	92	23	57	6.00	1
12	Cmpd05	[illegible]	60	21	22	92	23	57	6.00	1
13	Cmpd06	71	41	13	3	92	23	57	6.00	1
14	Cmpd09	[illegible]	41	22	15	92	23	57	6.00	1
15	Cmpd11	50	[illegible]	63	25	67	47	57	6.00	1
16	Cmpd18	[illegible]	54	22	32	92	23	57	6.00	1
17	marker_6.0	[illegible]	50	23	9	92	23	57		
18	Cmpd19	71	[illegible]	23	12	83	30	56	5.96	1.1
19	Cmpd10	61	42	24	5	83	20	51	5.75	1.8
20	Cmpd01	[illegible]	22	16	19	83	10	46	5.54	2.9
21	Cmpd04	[illegible]	25	24	29	83	10	46	5.54	2.9
22	Cmpd02	41	3	22	5	83	7	45		>3
23	Cmpd08	65	28	28	38	58	33	45		>3
24	Cmpd12	47	25	24	3	83	7	45		>3
25	Cmpd14	39	23	4	12	83	7	45		>3
26	marker_5.5	49	24	9	3	83	7	45		
27	marker_5.0	23	9	3	1	75	0	38		

Figure 16E

Fig. 16F

Table 2. The complete data set for 3 points and 3 colors, in systematic order.

compound	percent inhibition highest conc	--->	lowest conc	data group number highest conc	--->	lowest conc
cmpd 01	2	29	22	1	1	1
cmpd 02	15	10	38	1	1	2
cmpd 03	31	26	79	1	1	3
cmpd 04	21	46	25	1	2	1
cmpd 05	30	53	61	1	2	2
cmpd 06	17	37	70	1	2	3
cmpd 07	26	90	17	1	3	1
cmpd 08	10	90	38	1	3	2
cmpd 09	32	72	94	1	3	3
cmpd 10	34	17	15	2	1	1
cmpd 11	51	8	42	2	1	2
cmpd 12	56	3	69	2	1	3
cmpd 13	33	39	14	2	2	1
cmpd 14	53	52	55	2	2	2
cmpd 15	51	52	87	2	2	3
cmpd 16	65	82	6	2	3	1
cmpd 17	43	71	41	2	3	2
cmpd 18	65	99	77	2	3	3
cmpd 19	67	11	9	3	1	1
cmpd 20	87	5	66	3	1	2
cmpd 21	77	8	70	3	1	3
cmpd 22	78	36	0	3	2	1
cmpd 23	85	40	63	3	2	2
cmpd 24	83	57	88	3	2	3
cmpd 25	73	88	15	3	3	1
cmpd 26	69	85	35	3	3	2
cmpd 27	79	68	91	3	3	3

data group color

highest conc ---> lowest conc

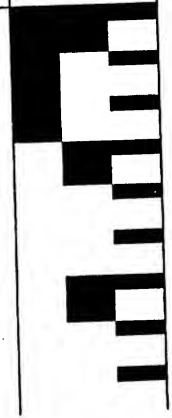


Fig. 16G

Table 3. The complete data set for 3 points and 3 colors, sorted by decreasing dose-responsiveness

compound	highest conc	--->	lowest conc	step scoring	unscaled score points	scaled responsive-ness 0-100
cmpd 22				+1+1	2	100
cmpd 10				+1+0	1	88
cmpd 13				0+1	1	88
cmpd 19				+1+0	1	88
cmpd 23				+1+0	1	88
cmpd 25				0+1	1	88
cmpd 26				0+1	1	88
cmpd 01				0+0	0	75
cmpd 14				0+0	0	75
cmpd 27				0+0	0	75
cmpd 04				-3+1	-2	50
cmpd 07				-3+1	-2	50
cmpd 08				-3+1	-2	50
cmpd 11				+1-3	-2	50
cmpd 12				+1-3	-2	50
cmpd 16				-3+1	-2	50
cmpd 17				-3+1	-2	50
cmpd 20				+1-3	-2	50
cmpd 21				+1-3	-2	50
cmpd 24				+1-3	-2	50
cmpd 02				0-3	-3	38
cmpd 03				0-3	-3	38
cmpd 05				-3+0	-3	38
cmpd 09				-3+0	-3	38
cmpd 15				0-3	-3	38
cmpd 18				-3+0	-3	38
cmpd 06				-3-3	-6	0

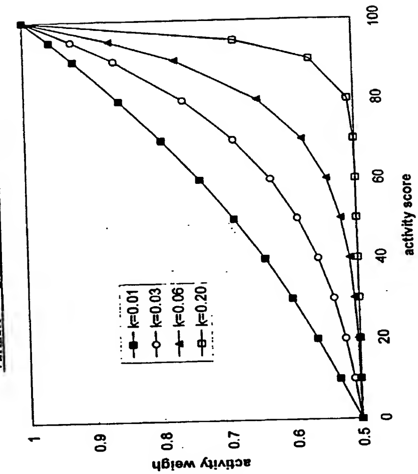
Fig. 16H

Table 4. The complete set of data for 3 points and 3 colors, sorted by decreasing overall activity.

	data group number			data group color					
compound	highest conc	--->	lowest conc	highest conc	--->	lowest conc	activity scoring	unscaled activity points	scaled activity 0-100
cmpd 27	3	3	3				1(3)+2(3)+3(3)	18	100
cmpd 18	2	3	3				1(2)+2(3)+3(3)	17	92
cmpd 24	3	2	3				1(3)+2(2)+3(3)	16	83
cmpd 09	1	3	3				1(1)+2(3)+3(3)	16	83
cmpd 26	3	3	2				1(3)+2(3)+3(2)	15	75
cmpd 15	2	2	3				1(2)+2(2)+3(3)	15	75
cmpd 17	2	3	2				1(2)+2(3)+3(2)	14	67
cmpd 21	3	1	3				1(3)+2(1)+3(3)	14	67
cmpd 06	1	2	3				1(1)+2(2)+3(3)	14	67
cmpd 23	3	2	2				1(3)+2(2)+3(2)	13	58
cmpd 08	1	3	2				1(1)+2(3)+3(2)	13	58
cmpd 12	2	1	3				1(2)+2(1)+3(3)	13	58
cmpd 25	3	3	1				1(3)+2(3)+3(1)	12	50
cmpd 14	2	2	2				1(2)+2(2)+3(2)	12	50
cmpd 03	1	1	3				1(1)+2(1)+3(3)	12	50
cmpd 16	2	3	1				1(2)+2(3)+3(1)	11	42
cmpd 20	3	1	2				1(3)+2(1)+3(2)	11	42
cmpd 05	1	2	2				1(1)+2(2)+3(2)	11	42
cmpd 22	3	2	1				1(3)+2(2)+3(1)	10	33
cmpd 07	1	3	1				1(1)+2(3)+3(1)	10	33
cmpd 11	2	1	2				1(2)+2(1)+3(2)	10	33
cmpd 13	2	2	1				1(2)+2(2)+3(1)	9	25
cmpd 02	1	1	2				1(1)+2(1)+3(2)	9	25
cmpd 19	3	1	1				1(3)+2(1)+3(1)	8	17
cmpd 04	1	2	1				1(1)+2(2)+3(1)	8	17
cmpd 10	2	1	1				1(2)+2(1)+3(1)	7	8
cmpd 01	1	1	1				1(1)+2(1)+3(1)	6	0

Fig. 16I

Variable Weighting of the Activity Score



10/048022

Fig. 16J

Table 5. The complete set of data for 3 points and 3 colors, sorted by decreasing composite score.

compound	highest conc	--->	lowest conc	scaled responsive-ness 0-100	scaled activity 0-100	composite 0-100
cmpd 27				75	100	100
cmpd 18				38	92	82
cmpd 26				88	75	80
cmpd 24				50	83	72
cmpd 23				88	58	72
cmpd 09				38	83	69
cmpd 25				88	50	68
cmpd 22				100	33	66
cmpd 14				75	50	62
cmpd 15				38	75	61
cmpd 17				50	67	60
cmpd 21				50	67	60
cmpd 13				88	25	56
cmpd 08				50	58	54
cmpd 12				50	58	54
cmpd 19				88	17	52
cmpd 10				88	8	48
cmpd 16				50	42	46
cmpd 20				50	42	46
cmpd 03				38	50	44
cmpd 07				50	33	41
cmpd 11				50	33	41
cmpd 05				38	42	40
cmpd 06				0	67	38
cmpd 01				75	0	38
cmpd 04				50	17	33
cmpd 02				38	25	31

Fig. 16K

Quality of Ranking when Noise = 10 Inhibition Percentage Points

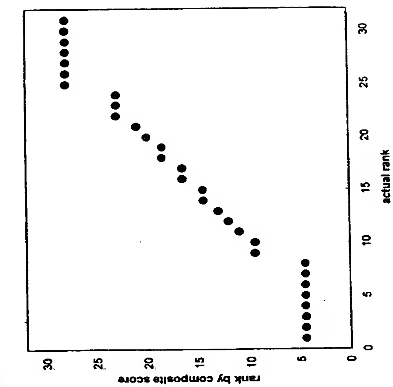


Fig. 16L

Quality of Ranking when Noise = 30 Inhibition Percentage Points

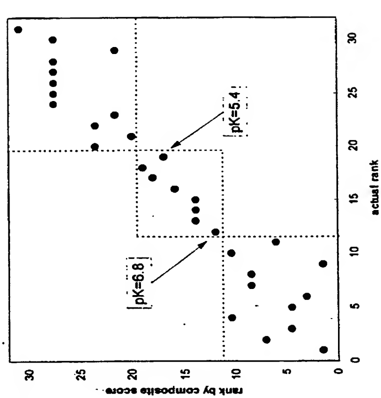


Fig. 16M

Table 6. Quantitative Estimation of Potencies by Calibration Marker Compounds

compound	% Inhib @ 3.00e-06	% Inhib @ 1.00e-06	% Inhib @ 3.00e-07	% Inhib @ 1.00e-07	D-R composite score	interp -log IC50	est IC50 μM
M353875	100	102	83	75	79		<0.1
marker_7.5	**99**	**97**	**90**	**76**	**79**		
M221211	110	91	69	39	76	7.00	0.10
M371585	108	102	63	27	76	7.00	0.10
marker_7.0	**97**	**91**	**75**	**50**	**76**		
M345077	102	87	92	87	75	6.97	0.11
M371796	91	78	76	33	73	6.90	0.13
M143629	100	79	48	43	69	6.77	0.17
M371890	101	72	42	29	69	6.77	0 17
M371891	92	69	55	49	69	6.77	0.17
M309032	105	62	62	21	67	6.70	0.20
M198289	101	82	38	18	66	6.67	0.22
M224602	97	79	43	23	66	6.67	0.22
M318671	93	63	42	14	66	6.67	0.22
M273373	95	93	52	25	65	6.63	0.23
M371336	78	70	44	27	62	6.53	0.29
M371825	61	64	60	26	62	6.53	0.29
M181250	99	46	46	36	61	6.50	0.32
M338331	87	73	29	15	61	6.50	0 32
marker_6.5	**90**	**76**	**49**	**24**	**61**		
M143630	65	28	28	38	60	6.44	0.36

Fig. 16N

Quality of Estimation when Noise = 10 Inhibition Percentage Points

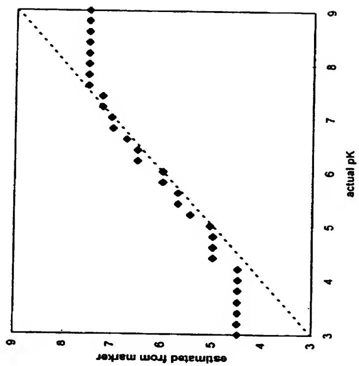


Fig. 16P

Quality of Estimation when Noise = 30 Inhibition Percentage Points

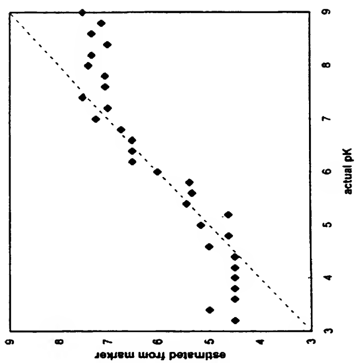
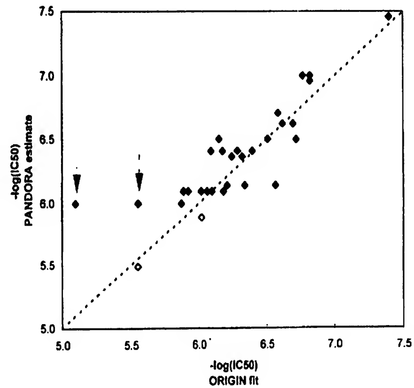


Fig. 16Q

Comparison of Curve Fitting to Marker Calibration
for T-cell Proliferation Data



	A	B	C	D	E	F	G	H	I
1	Cmpd	Series	Test1	Test2	Test3	HTS SPA Dose-Resp % Inhib @ 3x10-6M	HTS SPA Dose-Resp % Inhib @ 1x10-6M	HTS SPA Dose-Resp % Inhib @ 3x10-7M	HTS SPA Dose-Resp % Inhib @ 1x10-7M
2	Cmpd01	N		29	30				
3	Cmpd02	N		42	5.5	41	3	22	5
4	Cmpd03	G		2.61	11	83	57	28	15
5	Cmpd04	N			30	70	25	24	29
6	Cmpd05	N		1.8	9.2	89	60	21	22
7	Cmpd06	D	8.86	6.5	3.7	71	41	13	3
8	Cmpd07	D	3.11	0.037	7.8	100	79	48	43
9	Cmpd08	D		0.089	N.A.	65	28	28	38
10	Cmpd09	D	0.119			68	41	22	15
11	Cmpd10	N	0.233			61	42	24	5
12	Cmpd11	N	4.31			50	77	63	25
13	Cmpd12	H	1.3	0.24		47	25	24	3
14	Cmpd13	H	1.17	0.194	30	81	59	40	37
15	Cmpd14	H	0.26	0.41		39	23	4	12
16	Cmpd15	H	0.369	0.148		99	46	46	36
17	Cmpd16			0.87	30	101	82	38	18
18	Cmpd17	K		0.223	N.A.	81	64	47	24
19	Cmpd18		5.27			79	54	22	32
20	Cmpd19		0.134			71	71	23	12
21	Cmpd20			0.317		101	109	108	100
22	Cmpd21	K		2.21		87	70	31	13
23	Cmpd22	B		0.15		94	77	36	12
24	Cmpd23	B				96	61	36	12
25	Cmpd24	B	3.487	0.27	0.4	110	91	69	39

Figure 17A

10/048022

orig col	heading	# numeric	# text	# date	# blank	# total (longest col)	last occupied row num.	minimum (4 sig fig)	maximum (4 sig fig)	mean (4 sig fig)	standard dev (4 sig fig)	unique text strings and counts (24 different)
A	Cmpd		24			24	25					
B	Series		20		4	24	25					B (3) D (4) G (1) H (4) K (2) N (6)
C	Test1	12			12	24	25	0.119	8.86	2.385	2.726	
D	Test2	17			7	24	25	0.037	42	5.122	11.77	
E	Test3	10	2		12	24	25	0.4	30	15.76	12.59	N.A. (2)
F	HTS SPA Dose-Resp % Inhib @ 3x10-6M	23			1	24	25	39	110	77.57	20.43	
G	HTS SPA Dose-Resp % Inhib @ 1x10-6M	23			1	24	25	3	109	55.87	25.24	
H	HTS SPA Dose-Resp % Inhib @ 3x10-7M	23			1	24	25	4	108	35.52	21.85	
I	HTS SPA Dose-Resp % Inhib @ 1x10-7M	23			1	24	25	3	100	23.91	20.74	

* THIS COLORING INDICATES A DATA COLUMN WITH MIXED DATA TYPES

Figure 17B

	A	B	C	D	E	F	G
1	project name	most important factor scored by Mngr A	most important factor scored by Mngr B	most important factor scored by Mngr C	less important factor scored by Mngr A	less important factor scored by Mngr B	less important factor scored by Mngr C
2	Proj 01	2	[illegible]	2	1	2	2
3	Proj 02	1	1	1	2	1	2
4	Proj 03	1	1	1	1	2	1
5	Proj 04	1	1	1	1	2	1
6	Proj 05	1	1	1	1	1	2
7	Proj 06	2	1	1	1	2	1
8	Proj 07	1	1	1	1	1	1
9	Proj 08	1	1	2	1	1	1
10	Proj 09	1	1	1	1	2	1
11	Proj 10	2	1	1	1	1	1
12	Proj 11	1	1	1	2	1	1
13	Proj 12	1	1	1	1	1	2
14	Proj 13	1	1	1	1	1	2
15	Proj 14	1	2	2	1	1	1
16	Proj 15	2	[illegible]	2	2	2	2
17	Proj 16	1	2	2	1	2	1
18	Proj 17	2	1	[illegible]	2	2	2
19	Proj 18	1	[illegible]	[illegible]	1	1	1
20	Proj 19	2	2	2	1	1	1
21	Proj 20	1	2	1	1	1	2

Figure 18A

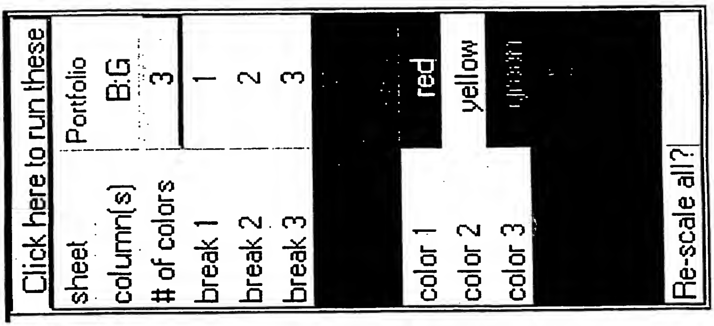

Click here to run these
sheet
Portfolio
column(s)
B:G
# of colors
3
break 1
1
break 2
2
break 3
3
color 1
red
color 2
yellow
color 3
Re-scale all?

Figure 18B

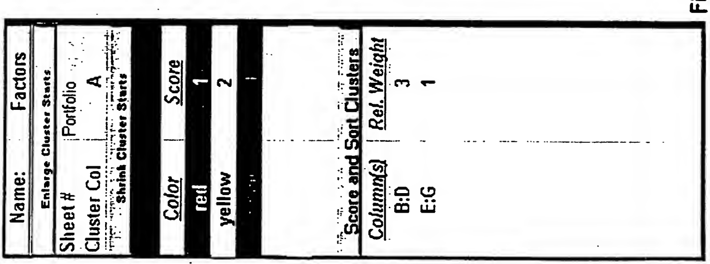

Name: Factors
Enlarge Cluster Starts
Sheet # Portfolio
Cluster Col A
Shrink Cluster Starts
Color Score
red 1
yellow 2
Score and Sort Clusters
Column(s) Rel. Weight
B:D 3
E:G 1

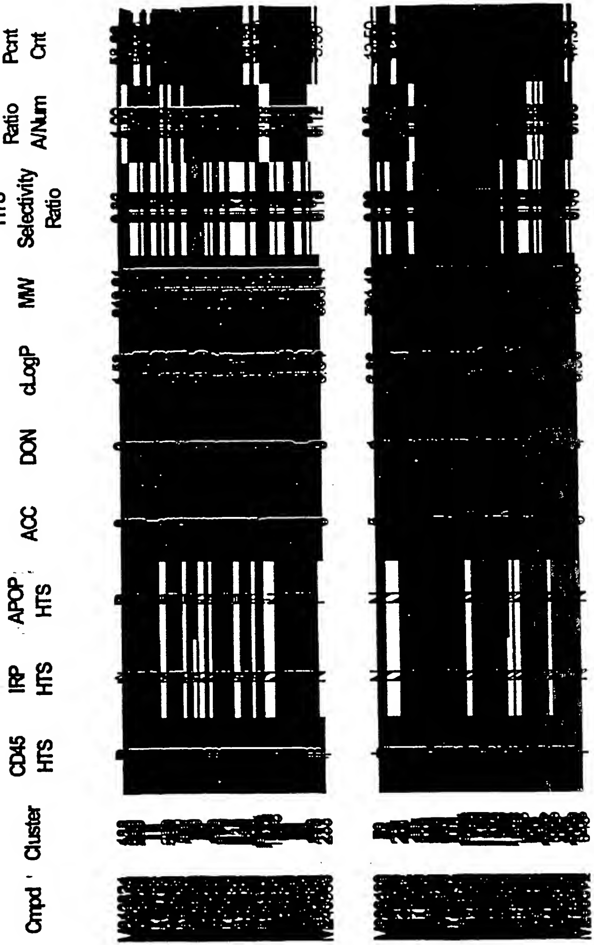
Figure 18C

	A	B	C	D	E	F	G	H
1	project name	most important factor scored by Mngr A	most important factor scored by Mngr B	most important factor scored by Mngr C	less important factor scored by Mngr A	less important factor scored by Mngr B	less important factor scored by Mngr C	score (0-100)
2	Proj 18	3	3	3	1	3	1	94
3	Proj 05	3	1	3	3	1	2	92
4	Proj 04	3	3	3	1	2	1	86
5	Proj 14	3	2	2	3	3	1	83
6	Proj 20	3	2	3	1	3	2	83
7	Proj 13	3	1	3	3	3	2	81
8	Proj 09	3	3	1	3	2	1	75
9	Proj 12	3	3	1	1	3	2	75
10	Proj 15	2	3	2	2	2	2	75
11	Proj 01	2	3	2	1	2	2	72
12	Proj 08	3	1	2	3	1	1	69
13	Proj 06	2	3	1	3	2	1	67
14	Proj 17	2	1	3	2	2	2	67
15	Proj 19	2	2	2	3	1	1	64
16	Proj 07	3	1	1	3	3	1	61
17	Proj 03	1	1	1	1	2	3	58
18	Proj 10	2	1	[illegible]	1	1	1	58
19	Proj 16	1	2	2	1	2	[illegible]	58
20	Proj 02	1	1	1	2	1	2	39
21	Proj 11	1	1	1	2	1	1	36

Figure 18D

Fig. 19

Drug Candidate Compounds;
Scored, Sorted, and Vertically Compressed



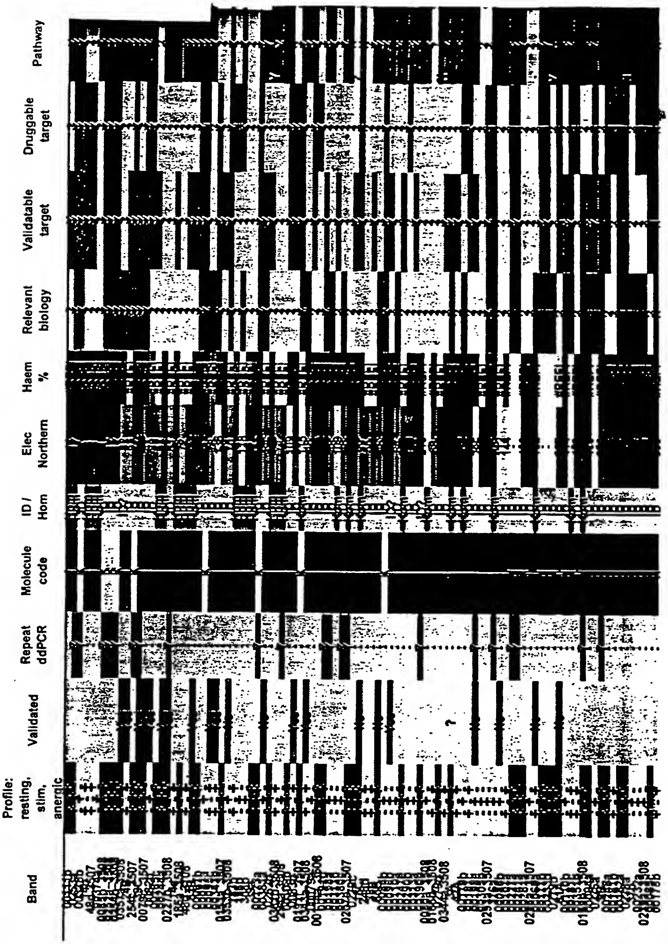


Fig. 20 Target Protein Candidates

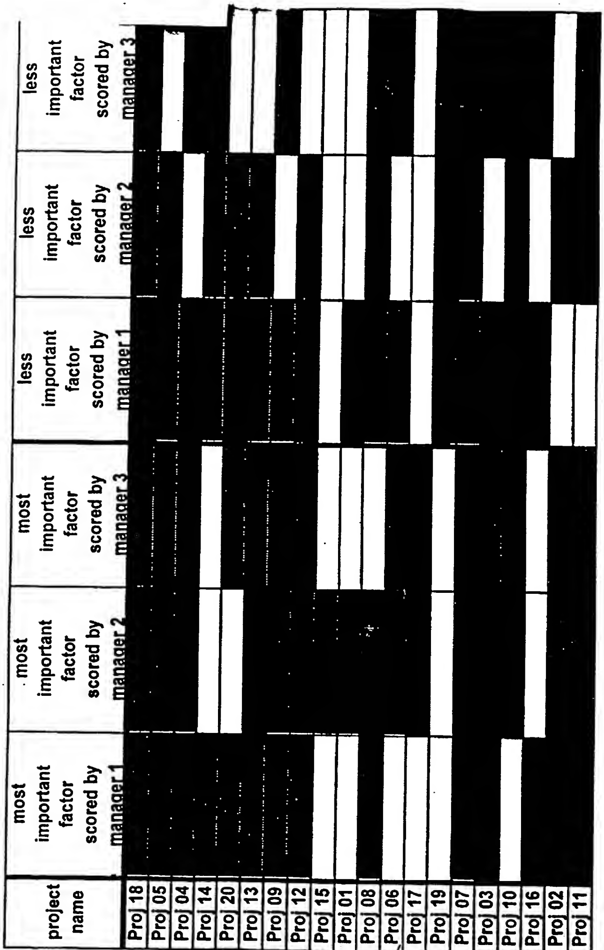

project name
most important factor scored by manager 1
most important factor scored by manager 2
most important factor scored by manager 3
less important factor scored by manager 1
less important factor scored by manager 2
less important factor scored by manager 3
Proj 18
Proj 05
Proj 04
Proj 14
Proj 20
Proj 13
Proj 09
Proj 12
Proj 15
Proj 01
Proj 08
Proj 06
Proj 17
Proj 19
Proj 07
Proj 03
Proj 10
Proj 16
Proj 02
Proj 11

Fig. 21

10/048022

Company	Disease 1	Disease 2	Disease 3	Disease 4	Disease 5	Disease 6	Disease 7	Disease 8	Disease 9	Disease 10	Disease 11	Disea 12
Company 1	Phase I		Phase II		LO/DE			LO/DE	Phase I		Phase II	Pha
Company 2	Phase I	LI	Phase II			LI/LO	LI/LO	LI/LO	LI/LO	LI/LO		
Company 3	LI/LO				LI/LO	Rx	LI/LO		Rx	Rx		
Company 4	LO				LO/Ph I	Phase II	LO	Phase II			LO	
Company 5	LI/LO			LO	LO	Phase I	LO/DE			LO		TS/
Company 6	LO		Rx	Rx				Rx				
Company 7	LI/LO							Phase I	LO/DE	LI/LO	Phase I	LI
Company 8	LO/DE	Phase II			LO				LO		LO	
Company 9	LI/LO					Phase I	LI/LO	LI/LO	LI/LO		LI/LO	LI/LO
Company 10		LO		LO	Phase III					Phase II		
Company 11	LO			LO	LO							
Company 12	LO		Phase II		LO							LI/LO
Company 13	LI				Phase III		Phase III					LI
Company 14	LI/LO		LI/LO		LI/LO			LI/LO			LI/LO	
Company 15	LI		LI	LI	LI					LI		
Company 16	LI		LI		LI		Phase II					
Company 17	Phase II				LI/LO	LI/LO						
Company 18			Phase II					Phase I				
Company 19	LI		LI				LI					
Company 20				LI/LO								
Company 21	LI/LO				PhaseI/II							
Company 22	TS		TS			TS				TS		
Company 23	LI				LO/DE							
Company 24	LI											
Company 25	LI/LO											

Fig. 22

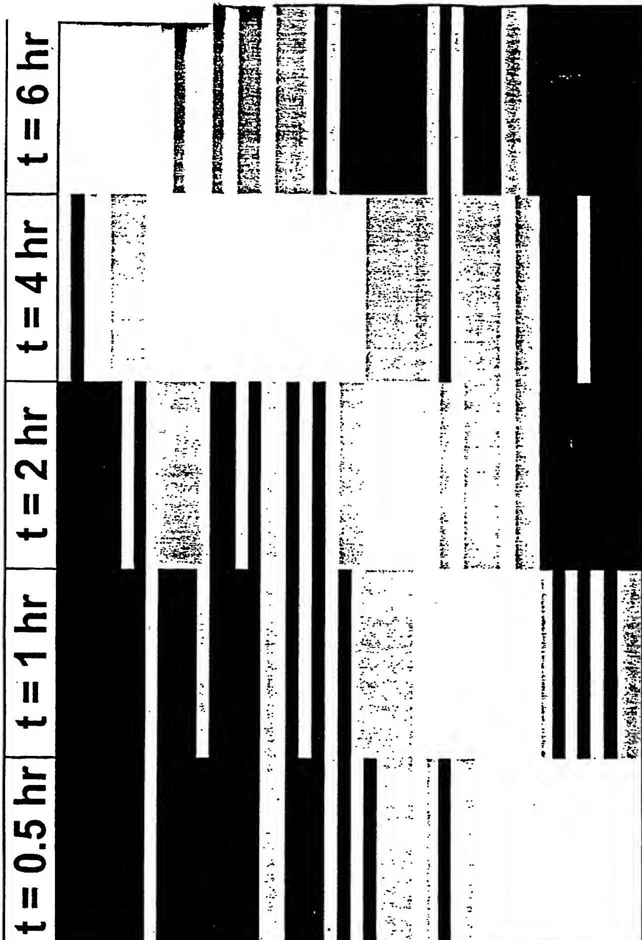


Fig. 23

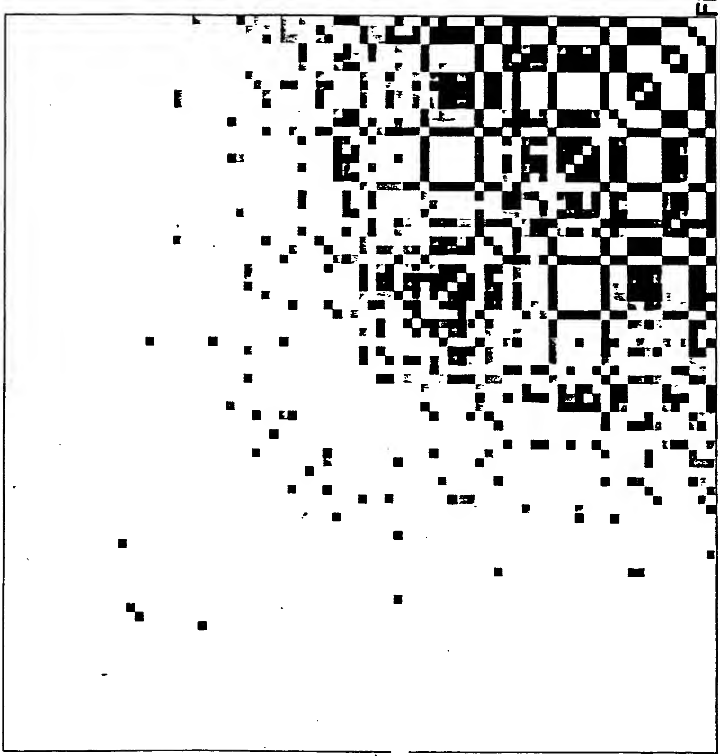


Fig. 24

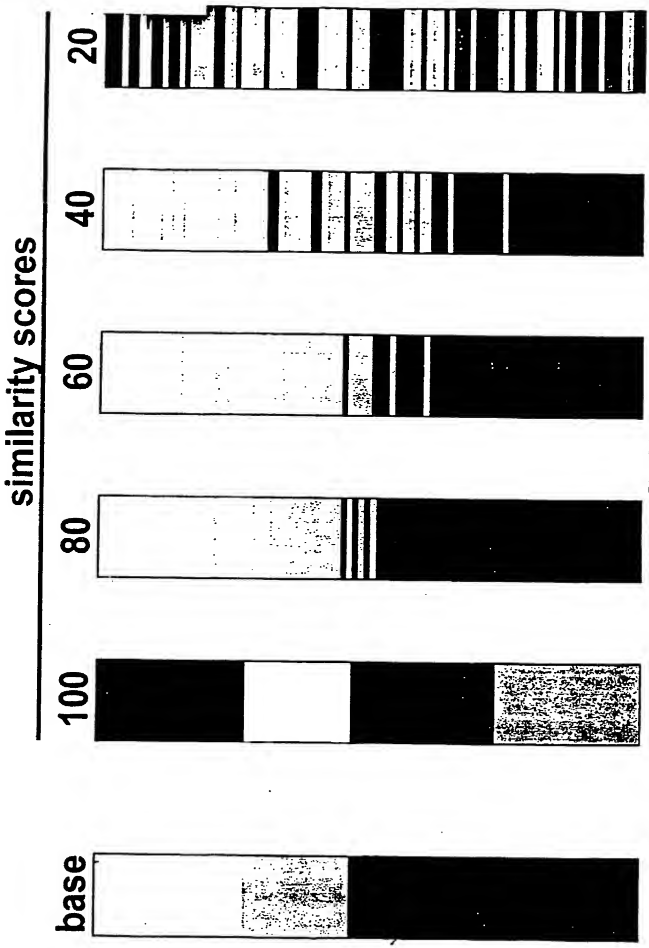


Fig. 25

COLOR GROUPING SIMILARITY SCORES	Col. C	Col. D	Col. E	Col. F	Col. G	Col. H	Col. I	Col. J	Col. K	Col. L
Col. B	19	100	19	82	[illegible]	37	53	53	21	19
Col. C		19	100	21	20	28	56	56	18	20
Col. D			19	82	[illegible]	37	53	53	21	19
Col. E				21	20	28	56	56	18	20
Col. F					71	43	54	54	20	19
Col. G						[illegible]	51	51	18	18
Col. H							52	[illegible]	15	17
Col. I								100	[illegible]	[illegible]
Col. J									50	[illegible]
Col. K										0

SIMILARITY
75 - 100
50 - 75
25 - 50
0 - 25

Fig. 26

FOR UTILITY/DESIGN
CIP/PCT NATIONAL/PLANT
ORIGINAL/SUBSTITUTE/SUPPLEMENTAL
DECLARATIONS

RULE 63 (37 C F R 1 63)
DECLARATION AND POWER OF ATTORNEY
FOR PATENT APPLICATION
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Z70564/UST

As a below named inventor, I hereby declare that my residence, post office address and citizenship are as stated below next to my name, and I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the INVENTION ENTITLED **ANALYSIS AND PATTERN RECOGNITION IN LARGE, MULTIDIMENSIONAL DATA SETS USING LOW-RESOLUTION DATA GROUPING.**

The specification of which (CHECK applicable BOX (ES))

BOX (ES)
A. ☐ Is attached hereto
B ☐ Was filed on ____________ as U S Application No ____________

C X was filed as PCT International Application No **On PCT/US00/20401 ON 27TH July 2000**

And (if applicable to U S or PCT application) was amended on ____________ I hereby state that I have reviewed and understand the contents of the above identified specification Including the claims, as amended by any amendment referred to above I acknowledge the duty to disclose all information known to me to be material to Patentability as defined in 37 C F R 1 56 Except as noted below, I hereby claim foreign priority benefits under 35 U S C 1 19(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate or 365(a) of any PCT International Application which designated at least one other country than the United States, listed below and have also identified below any foreign application for patent or inventor's certificate, or PCT International Application, filed by me or my assignee disclosing the subject matter claimed in this application and having a filing date (1) before that of the application on which priority is claimed Or (2) if no priority claimed, before the filing date of this application

PRIOR FOREIGN APPLICATION (S) Number	Country	Day/MONTH/Year filed	Date first laid-open or published	Date Patented or Granted	Priority NOT Claimed
09/361122	US	27TH July 1999			

Except as noted below, I hereby claim domestic priority benefit under 35 U S C 119(e) or 120 and/or 365(c) of the indicated United States applications listed below and PCT international applications listed above or below and, if this is a continuation-in-part (CIP) application, insofar as the subject matter disclosed and claimed in this application is in addition to that disclosed in such prior applications, I acknowledge the duty to disclose all information known to me to be material to Patentability as defined in 37 C.F.R 1 56 which became available between the filing date of each such prior application and the national or PCT international filing date of this application:

PRIOR U.S. PROVISIONAL, NON PROVISIONAL AND/OR PCT APPLICATION (S) Application No. (series code/serial no.)	Day/MONTH/Year Filed	Status Pending, abandoned, patented	Priority NOT Claimed

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 16 of the United States Code and that such wilful false statements may jeopardize the validity of the application or any patent issued thereon

And I hereby appoint Pillsbury Winthrop LLP, Intellectual Property Group, telephone number (202) 861-3000 (to whom all communications are to be directed), and persons of that firm who are associated with USPTO Customer No 909 (see below label) individually and collectively my attorney to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith and with the resulting patent, and I hereby authorize them to delete from that Customer No Names of persons no longer with their firm, to add new persons of their Firm to that Customer No , and to act and rely on instructions from and communicate directly with the person/assignee/attorney/firm/organization who/which first sends/sent this case to them and by whom/which I hereby declare that I have consented after full disclosure to be represented unless/until I instruct the above Firm and/or an attorney of that Firm in writing to the contrary

00909

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